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MINNESOTA MEDICINE

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VOL. XVI NOVEMBER, 1933 No. 11

UNDULANT FEVER (BRUCELLIASIS)*

WALTER M. SIMPSON, M.S., M.D., F.A.C.P.
Dayton, Ohio

DURING the past five years, undulant fever has evolved from the obscurity of a clinical curiosity to the prominence of an important public health problem. The occasional sporadic cases which were encountered prior to 1926 were for the most part related to endemic foci of goat infection in Texas, New Mexico and Arizona. Up to that time it appeared to be an established fact that undulant (Malta) fever had its sole source in goats and was transmitted to human beings through the ingestion of their raw products.

The first recognition of the disease along the Mediterranean Coast produced such synonymous designations as Malta fever, Mediterranean fever, Gibraltar fever, rock fever, Neapolitan fever and Cyprus fever. In 1886, David Bruce[7] isolated the organism responsible for the infection; he named the organism *Micrococcus melitensis*. Some eleven years after Bruce's discovery, Bang[3] of Copenhagen, isolated the causative organism of contagious abortion of cattle, which he called *Bacillus abortus*. A British Commission, headed by Bruce, investigated the disease on the island of Malta during the years 1904 to 1907. They demonstrated that the ingestion of raw goat's milk was the common source of infection for man. The prohibition of the use of raw goat's milk by the men of the military and naval forces produced an immediate and rapid decline in the incidence of the disease.

For twenty-one years the *Micrococcus melitensis* of Bruce and the *Bacillus abortus* of Bang were regarded as separate, unrelated species, until Alice Evans,[12] in 1918, discovered that the two organisms were indistinguishable morphologically, biochemically, culturally and by ordinary agglutination tests. The results of further studies led Evans to state that the two organisms probably possessed similar pathogenicity for human subjects. In 1927, Carpenter[8] recovered an organism indistinguishable from *Brucella abortus* from the blood of ten human beings with undulant fever; five pregnant heifers inoculated with these cultures promptly aborted. These observations of Evans and Carpenter have been confirmed by many workers throughout the world. It is now known that the organism which produces contagious abortion in cattle and other domestic animals is capable of producing in human beings a disease clinically and bacteriologically similar to the Mediterranean type of Malta fever.

American physicians soon realized that these observations provided an explanation for their failure to arrive at a confirmed diagnosis in many cases of typhoid-like and malaria-like diseases. Reports of the discovery of the disease in many widely separated states soon appeared. In 1926, forty-six cases were reported, chiefly from New York, Michigan, Illinois and Ohio. During the years 1927 to 1930, inclusive, the recorded cases numbered 217, 649, 1301 and 1385, respectively. During 1929, cases of undulant fever were recorded by state health departments in every state of the Union. During the past two years over 3000 cases of undulant fever have been officially reported to state health departments. Undulant fever is now a reportable disease in forty states.

During the past five years the writer has investigated 142 cases of undulant fever in Dayton and the surrounding communities. This undertaking was the result of a determined effort to learn of the incidence of the disease in a circum-

*From the Diagnostic Laboratories of the Miami Valley Hospital, Dayton, Ohio. Presented before the General Assembly of the Minnesota State Medical Association, Rochester, May 23, 1933.

scribed locality. Stimulated by a similar motive, Hardy[21] has investigated over 800 cases in Iowa, during the past four years. Carpenter[10] in New York, Huddleson [22] in Michigan, Bierring[4] in Iowa, King[24] in New York, Farbar and Mathews[16] In Indiana, Brown[6] in Kansas, Sensenich and Giordano[29] in Indiana, and Ey[14] in Ohio, have conducted similar investigations in their localities; their efforts have likewise been rewarded by the discovery of a large number of cases. The inference is obvious that the disease must be much more prevalent than is generally believed.

The findings of Evans made it apparent that the *abortus-melitensis* group of organisms should be reclassified. Meyer and Shaw[20] proposed that the organisms of this group should be designated by the generic name *Brucella;* this suggestion has met with universal approval. It is believed by some that there are three varieties of *Brucella.* The organism usually associated with infection in goats has been designated as *Brucella melitensis* variety *melitensis;* the organism of contagious abortion of cattle is referred to as *Brucella melitensis* variety *abortus;* the organism ordinarily found in swine infections has been called *Brucella melitensis* variety *suis.* The *Brucella* exhibit marked pleomorphism; coccoid and bacillary forms, as well as intermediary oval forms, are commonly observed. Attempts to divide the organisms of the genus *Brucella* into distinct caprine, bovine and porcine species (by cultural characteristics, serologic reactions, pathologic changes, hydrogen sulphide metabolism, bacteriostatic action of dyes, utilization of dextrose and agglutinin absorption tests) have not been uniformly successful. Organisms which have been designated as porcine or caprine species have been recovered from cow's milk. In the light of present knowledge it seems desirable to refer to all of the varieties as the *Brucella.* Furthermore, the confusion resulting from the many names which have been used to designate the disease caused by *Brucella* in animals and man would be overcome by the adoption of the single designation *Brucelliasis.*

Among urban populations the disease appears to be chiefly transmitted through the raw milk of cattle infected with the *abortus* variety of the organism. Of the 142 cases of undulant fever studied by the writer, the ingestion of raw milk containing the organism of contagious abortion of cattle was demonstrated to be the source of infection in the great majority of instances; these findings are corroborated by the investigations of Carpenter, King, Orr, Huddleson, Farbar, Mathews, Sensenich, Giordano, Ey and others. Hardy expresses the belief that direct contact with infected cattle and hogs has been responsible for a great number of cases of undulant fever occurring in that State. Hardy's investigations lead him to the conclusion that the *abortus* and *suis* varieties of the organism are about equally responsible for the undulant fever morbidity in that State. Hardy[20] has demonstrated by animal experiments that the skin may act as the portal of entry of the organism. Morales-Otero,[27] of Puerto Rico, has reproduced the disease in human volunteers by inoculations with bovine and porcine strains of *Brucella abortus* through abraded skin. It is apparent, therefore, that there are two important sources of infection for man, namely, the ingestion of raw milk or unpasteurized dairy products containing *Brucella,* or direct contact with infected fresh animal tissues.

CLINICAL MANIFESTATIONS IN MAN

Because undulant fever presents many symptoms and signs common to typhoid fever, malaria, tuberculosis and influenza, it is frequently confused with these diseases. Many physicians have arrived at a tardy diagnosis of undulant fever only after repeated negative Widal reactions, the failure to demonstrate the malarial plasmodium, and the inability to elicit physical signs or roentgenographic evidence of tuberculosis. Less often, the disease has been confused with acute rheumatic fever, subacute bacterial endocarditis, bronchitis, pyelitis, appendicitis, cholecystitis, or tularemia.

As a result of the more extensive studies which have been made during the past few years, it has become increasingly apparent that a majority of the cases of undulant fever present a more or less characteristic clinical picture. The disease appears to occur predominantly among males, particularly in rural districts. Young and middle-aged adults are most often affected. Children appear to possess some degree of immunity to the disease; ten per cent of the patients in the Dayton series of cases were children in the first decade of life. The relative immunity of children appears to parallel that of calves.

The incubation period has been found to vary from five days to three weeks; the average incubation period is two weeks. The prodome is not unlike that of any general infection, although in occasional cases the disease is initiated with a chill and a rapid elevation of temperature to 103-105° F. Ordinarily, the patient becomes gradually aware of an afternoon or evening rise of temperature, associated with chills, nocturnal perspiration and marked weakness. The fever, chills and sweats usually pursue a characteristic course. The patient usually feels quite well in the morning, particularly in the early stages of the infection. As the daily elevation of temperature develops, usually during the afternoon or evening, the symptoms return. The nocturnal exacerbations of fever occasionally reach great heights (106-107° F.). The average maximum fever is 103° F. There is often a remarkable disparity between the subjective sense of feverishness and the extent of fever as registered by the clinical thermometer; in many instances the patient does not complain of fever nor does he present a febrile appearance, but the physician finds, to his great surprise, a fever of 102 to 103° F. As the fever abates, chills and sweating occur. If defervescence is rapid, the perspiration is more likely to be of a drenching character. The chills are sufficiently severe to be regarded as true rigors in about one-third of cases. There has been no history of chills in about ten per cent of patients who have experienced fever and sweats.

Marked restlessness and insomnia usually accompany the nocturnal febrile exacerbations. Delirium occurs in some cases in which the fever reaches great heights. Ordinarily, the mental state remains clear during the febrile course of the disease; the so-called "typhoidal state" is rarely, if ever, observed.

The matutinal remissions and the nocturnal exacerbations of fever may last from one week to several months. The name "undulant fever" refers particularly to recurring relapses of fever. Such febrile relapses appear to be the exception rather than the rule in the recently described American cases; most patients have experienced but one febrile period, lasting from one week to several months, and finally reaching the normal level by lysis.

The essential gastro-intestinal complaints are anorexia and constipation. The degree of constipation appears to parallel the severity of the infection. Diarrhea is of rare occurrence. Loss of weight is an almost constant feature of the disease. Patients experiencing a severe infection will often lose from twenty-five to fifty pounds in weight.

With the exception of such signs as fever, weakness and loss of weight, there is often a remarkable absence of positive physical findings. The spleen is palpable in about one-third of the cases. Tenderness or pain in the joints, or muscles, or both, is likewise observed in about one-third of the cases. The presence of transient migrating polyarthritis, particularly of the larger joints, has led to confusion with acute rheumatic fever. No permanent impairment of the joints has been observed.

Probably the most important surgical consideration in undulant fever lies in the frequent occurrence of abdominal pain during the acute manifestations of the disease. Abdominal pain was a prominent feature of the disease in sixteen of the Dayton cases. Among 125 cases studied by Hardy, abdominal pain was present in forty; in ten of these it was the major complaint, and it was a marked feature of the disease in twenty-four others. In the cases studied by me the pain was localized in the epigastrium in six instances, in the right upper quadrant in four, and in the right lower quadrant in six. In four instances of sudden right lower quadrant pain with fever, appendectomy was performed. In one instance a gangrenous appendix was found; this patient had been ill with an intermittent fever for three weeks prior to the development of acute pain in the lower right abdominal quadrant, associated with muscle rigidity over McBurney's point. A leukocyte count made at this time showed 6,000 leukocytes, 62 per cent of which were polymorphonuclears, the other white cells being equally divided between small and large lymphocytes. The development of acute appendicitis as a complication of undulant fever is practically unknown. This exceptional case was made the subject of a report by L. G. Bowers and the writer.[32] In the other three cases in which appendectomy was performed normal appendices were removed. In these three cases the surgeons requested the agglutination test for undulant fever after operation in an effort to find the real cause of the abdominal pain and persistent fever. After the agglutination test was reported positive

a typical undulant fever history was elicited in all three of the cases. In two of the Dayton cases cholecystectomy was seriously contemplated because of the existence of upper right quadrant pain, associated with fever, chills and sweats. Leo Ey[15] has recently stated in a report of thirty-five cases of undulant fever that one of the patients was operated upon for appendicitis, one for cholecystitis, while another was being prepared for similar operation when the real cause of his illness was discovered by the agglutination test. The writer has learned of twenty-one other instances in which appendectomy has been performed and eight in which cholecystectomy has been performed upon patients suffering from undulant fever. The pathologic studies of the appendices and gallbladders in these cases revealed no evidence of any active inflammatory process. These findings lead to the conclusion that many patients with undulant fever will present some clinical symptoms and signs which might easily be attributed to appendicitis or cholecystitis. It becomes a matter of some importance, therefore, that the surgeon should be aware of the characteristics of this disease in order to avoid unnecessary surgical interventions.

Brucella abortus exhibits a predilection for the genital tract of cattle. There is convincing evidence that the same selectivity occurs in some human beings. Painful swelling of the testes was a prominent feature of the disease in twelve of our cases and in forty of Hardy's cases. The elimination of the organism in the urine has been a common finding. In the bull, the infection frequently gives rise to seminal vesiculitis and orchitis. In guinea pigs which are inoculated with *Brucella abortus,* orchitis is a common result. Three of our male patients were first examined by genito-urinary surgeons who found clinical evidence of seminal vesiculitis, prostatitis, epididymitis and orchitis. All three denied exposure to gonococcal infection and repeated smears made from uretheral discharges after prostatic massage revealed no gram-negative diplococci. The sera of the three men was found to agglutinate *Brucella abortus* in dilutions from 1:160 to 1:640. Furthermore, the organism was recovered in one case from a draining sinus tract which extended from the globus major of the epididymis through the scrotal wall. Two of these patients were constant consumers of raw milk; the third drank raw milk occasionally and used unpasteurized country butter at his home.

The causative organism derives its name (*Brucella abortus* or organism of contagious abortion) from its etiologic association with abortion in cattle and other domestic animals. It seems reasonable to suppose that the organism might have a similar effect on pregnant women. The literature contains a number of reports of human abortions occurring on farms where the cattle were affected with contagious abortion. We have encountered five cases in which women who have repeatedly aborted and who presented no clinical or serologic evidence of syphilis, gave serologic evidence of previous infection with *Brucella abortus.* In these cases the agglutination titers ranged from 1:80 to 1:320. Four of the five women gave histories of a previous febrile illness, the nature of which had not been determined, at intervals from three to six years previously. All had been raw milk consumers. *Brucella abortus* has been isolated from a tubo-ovarian abscess which developed as a late complication in a case of known undulant fever. Kristensen[25] isolated the *abortus* variety of the organism from the exudate which covered the uterine site of the placenta of a seven-month fetus. Carpenter[9] has recovered the organism from the tissues of a human fetus which was aborted at the end of the fourth month of gestation. Frei[18] has isolated *Brucella* organisms from the vaginal discharge of a woman who had aborted ten days previously. Other investigators, notably Harbinson,[19] and Ey, have found strongly circumstantial serologic evidence that *Brucella* infection was a factor in the production of several cases of human abortion. These findings open a new field of investigation in cases of human abortion.

A skin eruption, usually macular or maculopapular, is a relatively infrequent finding; the skin lesions may simulate the roseola of typhoid fever.

Hematologic studies usually yield important information. Some degree of secondary anemia, usually proportionate to the severity of the illness, is almost invariably present. The great majority of cases exhibit leukopenia, with the white blood cell count ranging from 4,000 to 6,000. A relative, and in some cases an absolute, lymphocytosis usually accompanies the leukopenia. Occasional patients with the mild form

of the disease show very little deviation from the normal as regards the blood picture.

The urinalysis usually reveals the trace of albumin commonly found in febrile diseases. The cerebrospinal fluid may show slight lymphocytosis and an increased sugar content, but in most cases shows no abnormalities.

CLINICAL TYPES

Four types of the disease are generally recognized: (1) intermittent, (2) ambulatory, (3) undulatory, and (4) malignant.

(1) *Intermittent type.* The majority of cases which have been observed in the United States fall into this group. The disease pursues a subacute course, with fever of an intermittent character; the morning temperatures vary from normal or slightly subnormal to 100° F., while the evening temperatures usually range from 101 to 104° F. The average duration of this type of the illness is from three to four months.

(2) *Ambulatory type.* Approximately one-fourth of the cases are characterized by a relatively short and mild illness. Many persons in this group will remain at their work although aware of the existence of mild fever and a marked sense of weakness. The symptoms and signs of this form of the disease are essentially the same as in the intermittent type, except that they are much less severe. Such cases are frequently confused with influenza.

(3) *Undulatory type.* This form of the disease is characterized by the occurrence of relapses. This feature of the disease was said to be of frequent occurrence in the Mediterranean cases, but has been present in only about 15 per cent of the cases which have occurred in this country. The successive relapses usually decrease in intensity and duration. Such cases usually pursue a more chronic course than the other forms of the disease. Physical and mental deterioration are more commonly observed in the undulatory form of the disease than in the other forms.

(4) *Malignant type.* This form of the disease is rare, having occurred in only about 2 per cent of the cases reported in this country. A sudden onset, an acute course with extreme hyperpyrexia and a fatal termination in the majority of cases are the characteristics of this unusual form of the disease. The duration of this type of the disease is usually from one to three weeks.

DIAGNOSIS

If undulant fever is given consideration in the differential diagnosis of all cases of febrile illness, especially in those in which the diagnostic criteria for typhoid fever, tuberculosis, influenza, malaria, chronic bronchitis, pyelitis, rheumatic fever or bacterial endocarditis are not convincing, the disease will be recognized with much greater frequency. This is true in cases of vague mild febrile disease as well as in those in which the clinical manifestations of undulant fever are more clearly defined. In such cases it should become an established practice to submit 4 or 5 c.c. of the patient's blood, collected exactly as for the Wassermann test, to a laboratory equipped with the proper antigens, for the agglutination test. The rapid macroscopic agglutination method of Huddleson[23] is a simple and reliable procedure.

Anti-*abortus* serum agglutinins may appear as early as the fifth day, but in most instances they appear sometime during the second week of illness. It is, therefore, unwise to collect the blood specimen for the agglutination test until a week or ten days after the onset of illness. In occasional cases agglutinins will not appear until the third or fourth week of illness. The agglutination titer rises to variable heights during the acute course of the disease and tends to fall when the fever abates. Ordinarily, agglutination in dilution of 1:160 to 1:1280 will be found during the fourth or fifth week of illness. Many persons will retain anti-*abortus* serum agglutinins for many months or years, while in other cases they will entirely disappear a few months after recovery.

There is convincing evidence that about 5 per cent of individuals with undulant fever, from whose blood the organism may be recovered, fail to develop anti-*abortus* serum agglutinins. Furthermore, some patients who exhibit a well-defined clinical picture of undulant fever, and from whose blood *Brucella abortus* has been recovered, will show agglutination in titers below 1:80. It cannot be said, therefore, that there is any arbitrary diagnostic agglutination titer. For practical purposes, diagnostic significance is usually attributed to agglutination in dilutions of 1:80 or above. In patients in whom the clinical manifestations are strongly suggestive, the absence of agglutinins or the presence of agglutinins in titers of 1:10 to 1:40 should stimulate

further serologic and bacteriologic studies. The skin test, using an *abortus* antigen, appears to be of value in differentiating the cases in which agglutinins are absent or are present in low titer. This is done by injecting one-tenth of one c.c. of a saline suspension of heat-killed or formalin-killed abortus organisms, adjusted to a standard of two billion organisms per cubic centimeter. We utilize the same suspension for skin testing and for vaccine therapy. A positive test is characterized by the gradual development, usually within twenty-four to forty-eight hours after injection, of an indurated reddish area, usually about the size of a five cent piece. The induration usually persists for many days or weeks.

Subclinical *Brucella* infections have occurred in some persons who have been exposed to the infection; anti-*abortus* agglutinins have been demonstrated in the serums of such persons in the absence of clinical symptoms or signs of the disease. Carpenter, Boak and Chapman[11] have submitted convincing evidence that anti-*abortus* agglutinins develop only when there has been actual invasion of the tissues by living *Brucella* organisms.

The occasional cross-agglutination of the *Brucella* and *Bacterium tularense* should be borne in mind. Francis and Evans[17] have suggested that all serums from suspected cases of tularemia or undulant fever should be tested for both anti-*tularense* and anti-*abortus* agglutinins, unless the clinical history points definitely to a recognized source of infection for either undulant fever or tularemia. If it should develop that the *abortus* and *tularense* titers are the same, or nearly the same, agglutinin absorption tests will distinguish between them. The writer[30] has found *abortus-tularense* cross-agglutination in twenty-two of the 109 cases of tularemia and in twenty-eight of the 142 cases of undulant fever which he has investigated.

Since a bacteremia is present in this disease, an attempt to recover the organism by blood cultures should be made whenever possible. Blood for cultures should be collected early in the course of the disease and preferably at the crest of one of the pyrexial waves. The likelihood of recovering the organism is greater if broth mediums are inoculated directly; the carbon dioxid requirement of certain strains should be borne in mind.

Urinary specimens for culture should be collected through a sterile catheter. Amoss[1] has recently described a successful method for the recovery of *Brucella* organisms from feces. The same precautions should be exercised in disposing of the urine and feces of undulant fever patients as with those suffering from typhoid fever.

Guinea pigs may be inoculated intraperitoneally with the patient's blood or saline suspensions of macerated tissue. Six to eight weeks should elapse before autopsy. Loss of weight, the presence of enlarged joints, enlarged testes and seminal vesicles, small whitish foci of necrosis in the enlarged liver, spleen and lymphnodes should be noted. Cultures should be made from the lungs, liver, spleen, kidneys, testicles and lymphnodes.

PROGNOSIS

Fatal outcome is rare, having occurred in from 1 to 4 per cent of reported cases; during 1931, seventy-four deaths were officially recorded by the United States Public Health Service as having been due to undulant fever. The importance of the disease is not to be judged by the death rate. The prolonged course and resulting invalidism make the outlook much more serious than the death rate would indicate.

TREATMENT

The most important consideration in the control of undulant fever is prophylaxis. The widespread distribution of the infection among cattle renders it difficult to control the infection at its source. Many cows have Bang's disease and eliminate the organisms in large numbers in the milk and vaginal discharges without manifesting symptoms of the disease (abortion, mastitis, sterility and lessened milk yield). While veterinarians are striving to find more simple and effective methods to eliminate the infection among animals, there appears to be but one logical method for preventing the transmission of milk-borne infection to human beings, and that is by pasteurization. Park,[28] Boak and Carpenter,[5] and Zwick and Wedeman[32] have demonstrated that complete pasteurization (143-145° F. for thirty minutes) will destroy the *Brucella*. The need for strict supervision of the pasteurization process is apparent. For the protection of the health of those persons whose occupations bring them in direct contact with infected animal tis-

sues we must rely upon education and the institution of precautionary measures.

The rapidly accumulating knowledge of the widespread distribution of undulant fever has done much to focus the attention of public health workers, veterinarians and milk producers upon the urgent necessity of eliminating milk-borne infection among human beings. While some progress has been made in the control of the infection in certain herds by eliminating reactors, physicians and public health workers should be guided by the advice offered by Alice Evans:[13]

"For the protection of milk consumers the preventive measure is quite obviously the same as that practiced for the prevention of other infectious diseases that are spread by milk, namely, pasteurization. Those who are able to pay the price for certified milk may take raw milk with a reasonable degree of safety, *if the certification guarantees that the milk is from an abortion-free herd.* No milk other than that so certified, or pasteurized milk, can be considered safe, for the cattle disease is widespread everywhere in the United States. It is fortunate that the preventive measure of pasteurization is so easily available."

For those persons who live on farms, or in small communities in which pasteurization is not practiced, the milk should be boiled for five minutes or pasteurized by the simple vacuum-bottle method proposed by Arnold.[2]

The treatment of the disease in human beings has been essentially directed toward alleviation of the prominent symptoms. Mercurochrome, acriflavine, neoarsphenamin, quinine, and nonspecific protein therapy have been advocated by several physicians. For the most part these therapeutic observations have not been subjected to adequate control and the very length of the list argues against the specificity of any of these measures.

Many observers have reported favorable results with specific vaccine therapy. The writer has prepared and utilized a *Brucella abortus* vaccine, standardized to two billion heat-killed or formalin-killed organisms per cubic centimeter, in the treatment of seventy-two of the local cases, and has distributed the vaccine to some 400 physicians in various parts of the country, with results which appear to justify its use. Comparison with a series of untreated control cases appears to indicate that the vaccine usually terminates or shortens the course of the disease and prevents recurrence. Since undulant fever is often characterized by natural remissions, the value of any therapeutic measure must be interpreted with caution.

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THE RÔLE OF VITAMINS IN NUTRITION*

GEORGE O. BURR, Ph.D.
Minneapolis

ARE vitamins above suspicion? I have been reading "100,000,000 Guinea Pigs" by Arthur Kollet and F. J. Schlink. Although their picture of the American people as testers of unfit and poisonous foods may be exaggerated, there is much truth in the authors' contentions. It seems to me that vitamins have been made the excuse for many millions of guinea pigs. As you search through the advertising pages of any magazine, notice how many of the foods and tonics advertised offer richness in vitamins as their "raison d'etre." How much of this is justified, and what is the real place of vitamins in the plan for improving the health of humanity?

I will try to answer partially those questions by a résumé of our present knowledge of the vitamins and their effects upon metabolism. Since it is known that they exert a profound influence upon the body mechanism, it should always be kept in mind that the vitamins must be studied not as isolated forces, but in their relation to all metabolites. Like the hormones, food materials are so interrelated that they must be considered as parts of a complex whole.

A diet is now considered complete only when it contains balanced amounts of complete pro-

*From the Department of Botany, University of Minnesota. Presented before the annual meeting of the Minnesota State Medical Association, Rochester, Minnesota, May 23, 1933.

TABLE I. EFFECTS OF VITAMIN DEFICIENCIES*

Name of vitamin	Chemical characters	Richest sources	Results of deficiency
A "Antikeratic"	Fat-soluble Heat-stable (Carotene = provitamin A)	*Cod liver oil;* milk and dairy products; egg yolk; glands (especially liver); green leafy vegetables	Xerophthalmia; epithelial metaplasia; growth failure; emaciation; loss of vitality; sterility; urolithiasis; increased susceptibility to pyogenic infections (especially of visual, respiratory, digestive and genitourinary tracts), and (possibly) to neoplasms.
B (B_1) "Antineuritic"	Water-soluble Heat-labile (especially in alkali)	*Yeast;* whole grain cereals; fresh fruit and vegetables; egg yolk; glandular organs	Polyneuritis and (probably) human beriberi; paralysis; digestive disturbances; cardiac weakness; emaciation; growth failure; anemia; impaired lactation.
C "Antiscorbutic"	Water-soluble Heat-labile (Hexuronic acid?)	*Citrus* fruits; tomatoes; some other fruits and vegetables; sprouted grain	Scurvy; growth failure; lowered vitality; capillary degeneration; hemorrhages and anemia; impairment of teeth; skeletal, muscular and visceral degeneration; secondary infections.
D "Antirachitic"	Fat-soluble Heat-stable (Ergosterol = provitamin D)	*Irradiated ergosterol;* cod liver oil; egg yolk; irradiated foods; milk and butter	Rickets and osteomalacia; disturbance of calcium-phosphorus metabolism and ossification; dental caries; weakness and predisposition to infections.
E "Antisterility"	Fat-soluble Heat-stable	*Wheat germ* oil; whole grain cereals; green vegetables; muscle; glandular organs	Sterility, due to gonadal degeneration in male and imperfect placentation in female; embryonic death and resorption; muscular dystrophy; paralysis in young.
G (B_2 P-P) "Antipellagra"	Water-soluble Heat-stable	Yeast; liver; lean meat; milk, eggs; wheat germ; green vegetables	Pellagroid disorder in animals and (probably) human pellagra; dermal, digestive and neural lesions; weakness and growth failure.

*The author is indebted to Dr. C. M. Jackson, Department of Anatomy, for the use of this table. Only a few minor changes have been made.

teins (with all essential amino acids), digestible carbohydrates and fats, complete salt mixture and all the vitamins. Roughage is a usual constituent. There are at present six vitamins which are so well established that we know something about the effects of their absences from the diet. Many more factors are suspected as essential for the pigeon or for the rat. These have been given such names as B_3, B_4, B_5, Y-factor, Physin, et cetera.

It is an interesting commentary on our knowledge of the vitamins that although we know the pathological effects of their lack, we know practically nothing of their normal physiological activity.

Table I summarizes some information about the well established vitamins. They are listed alphabetically, and each vitamin is named after the pathological effect which is most specifically due to its absence. Most of the vitamins are so intimately associated with general body functions that they effect growth, nervous system and well being. A further grouping is often used, there being three water soluble substances (B, C and G) and three fat soluble (A, D and E).

Although until a few years ago no vitamins had been crystallized, such rapids strides have been made in the technic of micro-isolations that now possibly three are known in pure form—B, C and D.† Since some of these molecules are not extremely large, we may logically expect that in a short time some synthetic vitamins will be available. Already it is possible to substitute the yellow pigment carotene and irradiated ergosterol for vitamins A and D respectively. But when the above six vitamins are on the market in pure form, it will not be possible for animals to live on purified diets of protein, carbohydrate, fat. salts and the vitamins. Results with synthetic diets indicate that as purification takes place, the number of unknown dietary factors increases. Therefore, the best way to give an adequate diet is to supply a well diversified mixture of high grade natural foods—that is, plant and animal products which have received as little treatment and purification as possible.

It is true that the large part of nutritional research has been done on the young animal. This is the time of most rapid growth and development. Therefore, vitamin reserves are

†Since this was written, the isolation of vitamin A has been made by Karrer. The molecular structure of the vitamin is said to be established.

quickly exhausted and the effects of malnutrition are easily produced. From this work we know of the extensive malformations due to rickets, blindness following xerophthalmia, and poor growth due to low vitamin B. It is clear that the most critical test of nutrition is during the period of infancy, when the child is growing rapidly indoors and is dependent largely on a single food supply, milk. Although milk is the most complete and readily assimilated food known, still it is far from a perfect food. Among the well known deficiencies of milk are vitamins A, D and B and iron. The deficiency in B becomes more pronounced as the mother's diet is purified. It is now quite clear that an undernourished mother will either produce a milk of poor nutritional quality or will produce too little milk to satisfy the needs of the infant.

Of adults, the female is more likely to suffer than the male. This is due to the great nutritional demands of pregnancy and lactation. Shortages of calcium are most common. Except for this period of strain, adults are able to live for a long time on very deficient diets without noticeable effects. Since the average adult is capable of digesting a wide variety of dairy products, meats, vegetables, fruits and nuts, there would be no cause for worry about the adults' diet if it were possible to persuade people to eat a good selection of unpurified foods. The third column of Table I shows that a mixed diet made up of the above foods would be rich in all the vitamins and the probability of development of any known dietary deficiency on this diet would be small.

Two most valuable dietary constituents, sucrose and fat, become dangerous if consumed in too large quantity because they displace foods rich in good protein, minerals and vitamins. White flour and potatoes suffer from the same limitations. Therefore, it is quite possible even for adults to be undernourished while consuming adequate quantities of food. Herein lies a real danger. The adult does not quickly show effects of malnutrition which can be readily diagnosed. The trend of opinion of nutrition workers is that many people suffer from low vitality and high susceptibility to infection because they are not properly nourished. New methods of diagnosis of deficiencies of vitamin C have revealed large and unexpected numbers of sufferers from the lack of this fresh fruit and vegetable food-material. One of the greatest needs of nutrition today is methods of early diagnosis of small deficiencies. Our present information is largely based on extreme rat and guinea pig tests. We know almost nothing of optimum conditions for the human being.

Our safest course at present is to diversify the diet, including liberal quantities of milk products and fresh foods from land and sea. If this is done, there is little justification for making ourselves the guinea pigs for testing costly and uncertain products now advertised largely for their vitamin content.

THE SKIN MANIFESTATIONS OF AVITAMINOSIS*

S. E. Sweitzer, M.D.
Minneapolis

THE discovery of vitamins opened a study of extraordinary interest to medicine as a whole; the subject is a comparatively new one and is still in a state of flux, with new discoveries still being made.

When not enough vitamins are present in the diet certain pathological conditions result and certain diseases occur. McLester[5] gives as the deficiency diseases — xerophthalmia, beriberi, scurvy, rickets, osteomalacia, pellagra, simple goiter, xanthosis and general malnutrition, and of these certain ones show interesting dermatological conditions.

In xerophthalmia or keratomalacia, a disease due to a deficiency of vitamin A, Frazier and Ch'uan-K'uei Hu[4] reported some interesting observations. In the winter of 1928-1929 many cases of keratomalacia were seen in the Hospital of the Peiping Union Medical College. Most of these were Chinese soldiers who had been on a diet deficient in animal proteins and fats.

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In addition to the signs of keratomalacia, most of these patients showed certain cutaneous lesions of such uniform character as to suggest their being of more than coincidental significance.

Histological examination of the lesions in various stages of growth showed the pathologic process to be essentially one of hyperplasia and hyperkeratinization of the epithelium of the epidermis and hair follicles with associated metaplasia of the epithelium of the many sweat ducts to the keratinizing type, degeneration of the glandular structures of the skin, and infection.

Fig. 1. Pellagra. Backs of hands showing huge bullæ.

Histologically they were analogous to the pathologic changes seen in the eye and in other tissues of animals and man following deprivation of fat soluble vitamin A. As a rule these lesions preceded the eye symptoms and responded to dietary therapy simultaneously with the ocular lesions, although much more slowly.

Several weeks prior to the onset of the ocular symptoms the skin became dry and rough and later spinous papules appeared at the sites of the hair follicles. The upper and lower extremities were involved, also the shoulders, lower abdomen and, to a less extent, the chest, back and buttocks. The skin was darker than normal in some cases. There was absence of visible sweating and the articular folds, usually moist, were covered with dry delicate scales.

The follicular papules varied in size and each had as its apex a hard keratotic plug which projected above the surface of the lesions as a spinous process. The eruption was usually abundant and symmetrical.

Fifteen patients were observed and five of them showed extensive suppuration. Large numbers of comedones were present on the face but, unlike in acne, the skin was very dry.

From the fact that the histological changes in the skin resembled the changes seen in the eye, where there is cornification of the conjunctival and corneal epithelium, they assumed a strong probability of the specific nature of the cutaneous lesions.

However, Nicolau[6] and Willshire[8] described cutaneous changes essentially identical with their series of cases, as a manifestation of scurvy.

Frazier concludes that in correlating tissue changes with a specific vitamin deficiency, it should be remembered that single dietary faults rarely occur alone, inasmuch as a diet which is lacking in one factor is generally deficient in others.

In beriberi the only cutaneous change of note is edema.

Scurvy was the first disease that was recognized as having a dietary etiology. It has been known for many years and there is a voluminous literature concerning it. The commonly known skin manifestations are subcutaneous hemor-

rhages, bluish areas, also ulcerations and hemorrhages in the mouth.

Nicolau[6] described a follicular and perifollicular eruption in scurvy. He found a dry skin with numerous follicular hyperkeratoses on the extremities. Later pustulation can occur.

Fig. 2. Pellagra. Wrist showing sharp line of demarcation and heavily pigmented skin.

Willshire[8] studied 3,000 cases in Serbian troops. He found dryness of the skin, petechiæ, and follicular hyperkeratoses. The distribution was usually on the lower extremities but the upper extremities were also involved though to a lesser degree. He thought the pathologic changes were due to impairment of the follicular nutrition. Both Nicolau and Willshire stressed the value of these skin findings in making an early diagnosis of scurvy.

Xanthemia and Xanthosis.—Eating large quantities of vegetables and other foods which contain carotene and xanthophyll may lead to an accumulation of these pigments in the blood. This is called xanthemia and may in turn cause xanthosis, a yellowish pigmentation of the skin. This is most intense on the palms and soles and at the nasolabial folds. It occurs most often in diabetic and nephritic patients. We have had two such cases at the Minneapolis General Hospital. The condition has also been called carotinemia. Carotene and xanthophyll are normal constitutents of the blood and contribute to color the blood serum yellow.

Carotene is primary vitamin A and is converted in the body into vitamin A. Its toxicity has been tested and after extremely large doses have been given over a long period of time no deposit of yellow pigment has been produced in the skin. This suggests that this so-called xanthosis may be due to xanthophyll instead of carotene.

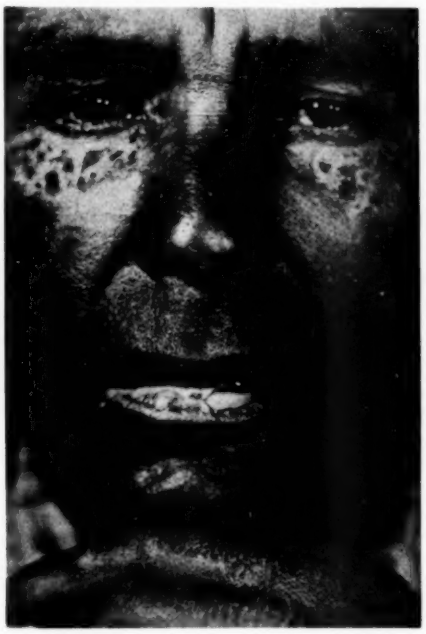

Fig. 3. Pellagra. Lesions on back of hand, face and lip.

Eusterman and Wilbur[9] have recently pointed out the versatility of vitamin A and have given an excellent review of the subject. Xanthosis is not, strictly speaking, a deficiency disease but seems to be due to some other metabolic disturbance with a pigment deposit in the skin. This pigment may be due to carotene or, what is more likely, to xanthophyll.

Pellagra.—Pellagra according to Crutchfield[2] is characterized by a bilateral, symmetrical, pigmented and scaly eruption which is preceded by erythema, edema and inflammatory infiltration.

Ormsby's description[7] is a classic. The eruption starts as a macular erythema which fuses and forms a patch of dermatitis almost identical with a sunburn. In a few days the color of the lesions deepens and they assume a reddish brown or chocolate hue. In from seven to ten days a

desquamation begins at which time a roughened, scaly surface is present. Early in the process there is moderate swelling. In the more active cases, on the erythematous base there develop bullous lesions which often attain huge size and which, after a few days, gradually dry leaving a thickened, crusted epidermis. Ecchymoses may complicate the process and secondary pyogenic infection may follow the vesicular or bullous cases. In severe cases ulceration may ensue and in many the edema is sufficient to cause fissures. Whether erythematous or bullous, the lesions are well defined. After the eruption has disappeared, the skin in some cases is pigmented; in others the pigment is lessened.

Fig. 4. Pellagra. Depigmentation of hands after bullæ were healed.

In certain cases where the process is less acute the appearance of a chronic dermatitis with marked hyperpigmentation is presented. After repeated attacks the skin becomes permanently thickened, hard, roughened, scaly and pigmented. The terminal stage is a thin, parchment-like scar, *i.e.*, atrophy.

The lesions are found on the exposed areas of the body chiefly, on the back of the hands, wrists, some parts of the face and neck. The feet and ankles are rarely involved here, but they are often seen in Europe where more people go barefooted. The arms and chest and, to a lesser extent, the ears and other parts of the body including the palms and genital region are also involved.

The lesions are strikingly symmetrical and the eruption on the hands and wrists has often been compared to that of a glove.

The sun seems to be a factor in determining the location of the eruption. In mild cases the tongue is red and swollen and presents smooth areas, especially at the tip and on the margins. In severe cases the tongue can show ulcerations which bleed easily. The buccal mucous membrane may also be involved.

From 1926 to 1932 inclusive there were observed at the Minneapolis General Hospital fifty-five cases of pellagra. These cases were all strikingly similar and all had the same etiological factors. They all were from the lowest human strata and all gave a history of long and excessive alcoholism. Most of them drank denatured alcohol; some used canned heat and obtained the alcohol from that. These patients all were seen in the summer months and the exciting cause was usually a more than ordinarily severe drunk and a subsequent sleep on the grass in the hot summer sun. These patients were all men and almost without exception admitted that, during their prolonged debauch, they ate very little, if at all.

The areas involved were the backs of the hands and wrists, sometimes the forearms, the face and neck. The tongue was usually red and swollen. Diarrhea was present in 25 per cent of the cases. Mental apathy was seen in only a few cases.

Clinically they were all characterized by a

severe edema of the backs of the hands and in almost every case bullæ were present. Sometimes these bullæ were so large as to lift the epidermis from the entire back of the hand. The bullæ were always infected and the areas involved were darkly pigmented. On resolution, a dry, dark, scaly skin was left.

Our treatment was wet antiseptic packs for the infected bullæ and high vitamin feeding. The lesions healed in from one to two weeks, and all the patients made a good recovery.

To test the effect of light, some of the patients were exposed to the ultraviolet lamp on areas of the body not involved with the disease, but, the results were negative. Patch tests of canned heat were also made in some cases but these tests were also negative.

In the year 1933 so far, two other cases of pellagra have been seen, both of the simple pellagra type. One of these men had been on a fairly good diet but had eaten a lot of canned food. He was in good physical condition except for the skin eruption and had no other symptoms. The other man was an old sheep herder who had been living on hardtack and bologna. He had a chronic type of pellagra with roughened, thickened skin over the hands and arms. There was no diarrhea but he was mentally upset.

This makes a total of fifty-seven cases of pellagra seen. All of them were males, fifty-five were of the alcoholic type and two were simple pellagra.

Boggs and Padget[1] analyzed the cases of pellagra seen at Johns Hopkins Hospital in the last twenty years. They divide pellagra into three classes: (1) the simple pellagras; (2) the post-alcoholic variety, and (3) pellagra arising as a complication of some other preceding disease. They observed no difference in the three types but considered them all as pellagra. Out of 102 cases they had forty of the alcoholic type, thirty-one of the simple type, and thirty-one complicating other diseases. They suggest that either the alcohol itself destroys the pellagra preventing factor in the gastrointestinal tract, or that the gastrointestinal tract is so altered by the large amounts of alcohol that it is incapable of assimilating the pellagra preventing factor.

My own opinion is that the alcoholic pellagras are real pellagras and that they are caused by lack of vitamins and especially vitamin G. These patients practically starve and in this they approach the pellagra caused by some other disease such as intestinal carcinoma.

One thing must be kept in mind when prescribing reducing diets. A long deprivation of certain essential foods may, in certain susceptible individuals, cause pellagra.

Conclusions.—In vitamin deficiency and nutritional disorders the skin is involved along with the rest of the other organs. It suffers in the same way and the symptoms can be largely explained on the grounds of a deprivation of some substance essential to the general body welfare.

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EYE MANIFESTATIONS OF AVITAMINOSIS*

D. L. TILDERQUIST, M.D.
Duluth

THE purpose of presenting this paper is twofold:

1. To give a brief summary of the eye manifestations of vitamin deficiencies.

2. To give the results of an investigation to determine the relative frequency of such eye disorders in the state of Minnesota.

The eyes are definitely affected by vitamin deficiency. Practically only one—Vitamin A—is involved. Recent work by O'Brien[10] offers an exception to this statement. He has produced cataracts of all types in young rats by the feeding of a diet free from Vitamin G (B^2, antipellagra). Whether or not the deficiency of Vitamin G is a factor in human cataract formation is not known. However, the symptoms as well as the underlying pathological changes resulting from Vitamin A deficiency are quite well determined, both in experimental animals and in humans. The most characteristic symptoms appear in the eyes and for this reason the diseases are of particular interest to the ophthalmologist.

Vitamin A seems to be necessary to keep epithelial tissues and tissues of epethelial origin "healthy," and the absence of Vitamin A affects such tissues, some more than others, in a characteristic way.[3] Cuboidal, cylindrical, or transitional cells change into the squamous keratinizing type; this change is not due to inanition but to a real metaplasia. The deepest cells of the layer are affected first and the process gradually extends to the surface. If this surface is exposed to the outside, as in the case of the epithelium of the respiratory tract or of the conjunctiva, infection often takes place and then symptoms, which up to this stage may have been absent, appear.

In the conjunctiva, the first stage is the disappearance of the goblet cells and later changes in the cells transform the epithelium and make the structure similar to epidermis. These changes manifest themselves at first by just a stickiness of the lids; later the conjunctiva becomes dry and white, and glistening spots appear (Bitot's spots), often covered with a whitish foam. Tears do not seem to moisten the spots and the surface acts as if it were greased. This condition is known as xerosis of the conjunctiva and cornea, or xerophthalmia. The conjunctiva becomes thick and lies on the eyeball in folds. Later the process advances in the cornea which becomes more cloudy; then there is a softening and breaking down of the corneal tissue, keratomalacia; and the ulceration advances until the cornea ruptures; infection takes place and there is finally blindness.

Pillat,[13] of China, describes two other symptoms which may appear independently of any other manifestations but only in individuals who have been exposed to partial Vitamin A deficiency for a long period: one, a mild dryness and cloudiness of the cornea, which he terms prexerosis, and the other a characteristic brownish-gray pigmentation of the conjunctiva which persists long after the Vitamin A deficiency has terminated.

Coincident with these eye changes, symptoms referable to the other epithelial tissues may be present, such as respiratory disorders, coryza, sinus infections, bronchitis, gastrointestinal symptoms, hematuria, etc.

Slowness of movements and mental sluggishness is mentioned and is explained by some involvement of nerve tissue on the basis that nerve tissue is of epithelial origin.

Night blindness or hemeralopia, meaning a normal vision in ordinary light but a much reduced vision in dimmed light, often occurs with or independent of other eye symptoms. This symptom is found in various diseases of the retina and optic nerve. Usually there are lesions which can be observed objectively, but in the case of night blindness from Vitamin A defiency, there are no changes of the retina demonstrable with the ophthalmoscope or in any other way. For this reason this form of night blindness is often termed idiopathic hemeralopia. Vision in dim light is largely dependent on the proper functioning of the periphery of the retina. Holm[6] demonstrated first in 1927 that the retina

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holds and stores comparatively large amounts of Vitamin A. Knowing that Vitamin A is a fat soluble substance and is associated with fatty substances, it is assumed that it is held by certain lipoids which are found in the retina only in the periphery.

Idiopathic hemeralopia[1, 2, 16] disappears promptly if Vitamin A is restored to the diet; xerophthalmia also disappears quite rapidly and corneal ulcers will heal, but if corneal tissue is destroyed, it will not be restored and cloudiness of the cornea will remain permanently.

These eye diseases due to malnutrition are not new but have been recognized as entities for a long time. Even Heroditus knew of idiopathic hemeralopia, and recommended as treatment "raw ox liver dipped in honey as much as he is able." During the Great War these diseases were found in larger or smaller groups of people which had become isolated for some reason and had been deprived of proper food supplies.

During the years from 1909 to 1920, inclusive, there were recorded more than six hundred cases of xerophthalmia and night blindness in Denmark. Blegvad,[2] a Danish ophthalmologist, in working over these records, first traced the cause to a lack of Vitamin A in the diet. His work furnishes a most fascinating story in the history of medical research.

Pillat,[11] of Peiping, China, in trying to determine the normal pigmentation of the conjunctiva in the Chinese, had great difficulty in finding Chinese individuals with normal conjunctivae because of the almost universal lack of Vitamin A in the Chinese diets.

Aykroyd[1] states that in the summer of 1929 he observed night blindness in New Foundland and Labrador in a group of people whose diet consisted of white bread, molasses, fresh cod muscle, salt meat, beans, peas, and some potatoes, with no milk, butter, eggs or green vegetables. Night blindness developed in less than a month on this diet. In those regions cod liver oil is strictly an article of export. All the cases were cured in from twelve to thirty-six hours by one or two doses of cod liver oil.

Riemer[16] reports the landing at Boston of a crew of nineteen sailors from a boat which arrived after a long voyage from the west coast of Africa. The crew had lived on a very similar diet to that just described and all the members suffered from malnutrition. There were two cases of night blindness and three cases of xerophthalmia.

In looking over the medical literature of the United States, there are otherwise very few cases reported. In 1927 a young man suffering from night blindness came to my office; after much investigation, the conclusion was reached that the lack of Vitamin A in his diet lay at the basis of the trouble. Although constantly on the lookout for similar instances, none has appeared since.

On the suggestion of Dr. Alvarez, an attempt has now been made to find out the relative frequency of these disorders in the state of Minnesota. For this purpose the following questionnaire was formulated:

I am attempting to determine the frequency of eye disorders in Minnesota and in neighboring states, due to deficiency of Vitamin A in the diet.

It would therefore be highly appreciated if you would indicate on the blank below whether or not you have seen any such cases. If you have, a brief statement of each case, giving especially the symptoms and findings as to the eyes and the nature of the diet used by the patient, would be of great value.

Number of cases of eye disorders traceable to malnutrition (specifically to Vitamin A deficiency in diet).

1. Xerophthalmia (dryness of conjunctiva and cornea)
2. Keratomalacia (cloudiness and softening of the cornea)
3. Hemeralopia (night blindness)

This questionnaire was sent to one hundred and twenty-five ophthalmologists and thirty-one pediatricians and internists in the state, a total of one hundred and sixty physicians.

Fifty-six replies were received. Forty-eight physicians had seen no cases. Nine physicians reported a total of seventeen cases (including my own) which in their opinions could be put under this classification.

In studying these reports, it was found that the cases naturally fall into two groups:

Group I.—Eye disorders associated with malnutrition, but complicated by other eye diseases (eleven in all).

Two cases of *retinitis pigmentosa* were reported. This disease seems to be of congenital origin, is characterized by night blindness and shows, as a rule, very definite retinal changes. One of these patients, a girl, aged six, with petit-mal, was placed on a ketogenic (high fat) diet with a remarkable improvement in vision.

Whether or not it was thought that Vitamin A had anything to do with this improvement was not stated.

Seven cases were reported as xerophthalmia or pemphigus. Ocular pemphigus is a rare disease and in common with general pemphigus has an unknown causation, but there is nothing to indicate that avitaminosis is a factor.

One case, a child eighteen months old, was diagnosed *keratomalacia.* No statement as to diet was made except that the child had had artificial feeding. It had always appeared weak. There were excoriations of epithelium and deep infiltrations of both corneæ, leading to final perforation and loss of the left eye. There existed also an increased intracranial pressure and a paralysis of the fifth nerve.

A pediatrician reported the case of a young child with malnutrition, cloudiness of the cornea and caries of the teeth. There were also mental deficiency and other congenital defects and he found it difficult to say how much of the eye trouble was due to malnutrition.

Group II. Cases of eye disorders due to malnutrition but without definite complications (six in all).

A girl baby, fourteen months of age, weighed four pounds at birth. She had been on a diet of lactic acid milk with addition of karo, and also on a diet of whole milk with dextro-maltose and had gained up to seven pounds. At the time of this illness, she was small, poorly nourished, and had bilateral corneal opacities and a staphyloma of each cornea. A purulent ophthalmia was also present in each eye. She had a respiratory infection and signs of rickets. In spite of all treatment, an evisceration of each eye finally had to be done.

One patient reported, a woman twenty-eight years of age, had dendritic ulcers of the cornea. She was very anemic and poorly nourished, having reduced her weight thirty pounds by means of a starvation diet. The usual local treatment was given and the patient placed on a diet rich in Vitamin A. In a few weeks the ulcers had healed completely—a very short course for dendritic ulcers.

In a girl of three and a half years, ulceration of the cornea had been present for two years in one eye and for two weeks in the second eye. Nothing was stated as to her diet, but she was given a nourishing diet with high Vitamin A content. Five weeks later the ulcers had healed.

A patient with xerophthalmia (age not given) whose diet had consisted mostly of carbohydrates, sweets, starches, no butter and no fats was given a diet of meats, liver, vegetables, and cod liver oil and became entirely well in three months.

In another case of xerophthalmia with stapyloma of the cornea and blindness there was no record of the diet except that it was inadequate as far as Vitamin A was concerned.

The author's case of hemeralopia is given below in detail.

In the first group, it is very difficult to evaluate the factor of malnutrition, since other eye diseases were present which could have produced the symptoms present. That leaves the second group—only six cases—for consideration.

There are two ideas gained from this investigation which seem to me to be of some value:

1. Eye disorders from Vitamin A deficiency are very rare in the state of Minnesota. This investigation is admittedly incomplete, but not as incomplete as one might at first glance suppose. It is true that the greater number to whom the questionnaire was sent did not respond; on the other hand, it can be safely assumed that these had no cases to report. It may be that some cases had not been recognized; but several physicians who reported having seen no cases added that they had seen cases of this nature elsewhere. Considering that this survey likely covers a period of from five to ten years, it traces only about one case per year out of Minnesota's population of over two million. In spite of the reports of suffering from lack of food during the present period of depression, our people must have been fed quite well.

2. Some eye disorders that are not now thought to be due to Vitamin A deficiency may be favorably influenced by the use of food rich in Vitamin A, and there is justification for trying this diet in chronic diseases such as retinitis pigmentosa, dendritic ulcers and others.

Grateful acknowledgment is hereby made to those of my fellow physicians who so kindly cooperated with me in this survey.

The following report of a case of hemeralopia is given:

N. M., male, aged twenty-one, came to me on June 20, 1927, complaining that he could not see at night. He first noticed difficulty in driving a car at night in

that he could not see the road. Later on he found that he could not see anything after dark. He could not see the door of the garage nor even the barn. He was compelled to give up being out-of-doors at night. In the daytime his vision was good and caused him no trouble in reading excepting when he read a great deal. He had no inflammation or redness of the eyes excepting occasionally when driving a car in the wind. In every other way he was well and "strong as an ox" and had no difficulty of any kind.

His habits were good: he did not smoke or use alcohol. He had not taken medicines of any kind previous to the onset of this trouble. According to his own statement, his dietary habits were good—he "ate everything."

His past history was entirely negative. He was employed by his father in the grain and feed business. His father and mother were living and well, and four sisters also.

The patient was a large man, well nourished and weighed about 180 pounds.

His eyes were entirely normal objectively; the media clear; fundi entirely normal; vision in each eye 20/20+. There was no refractive error of any importance. The fields were taken carefully and were found to be markedly contracted on all sides both to light and to colors. He could see all colors and they were present in their normal order.

There was nothing to explain his trouble. At a second visit, a much more careful inquiry as to the diet was made but nothing definite could be elicited, excepting that he admitted that he never ate liver. In spite of this, he was ordered to take cod liver oil, to eat liver and to take butter and cream and eggs in addition to his ordinary diet.

Shortly after that a sister of his came into the office and from her an entirely different story was obtained. She stated that the patient was the only boy in the family and that he had always had his own way and had been allowed to eat anything he pleased. His diet ever since childhood had been about as follows: He ate sweets in great amounts, candy, jelly, cookies, cake, but never pie. He liked hot rolls and often would eat as much as a panful at a time and drink large amounts of black coffee with them. Of meats, he took only pork which he liked in the form of chops and ham. Occasionally he would accept other meats but then only when fried very hard. He was very fond of peanut butter but avoided butter and cream; he drank milk only in small quantities and then only if it was very thin. He ate no eggs. He refused all vegetables and fruits as well, excepting occasionally a banana or an apple.

If this diet is examined, we find that it contains very little of Vitamin A.

How any child could choose by instinct, or perversity, a diet so as to avoid Vitamin A so effectually is hard to understand.

A report of this patient received in April, 1933, states that after his last visit he increased the variety of his diet and that his night blindness disappeared promptly and had not returned at any time since.

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SYSTEMIC MANIFESTATIONS OF AVITAMINOSIS*

HARRY OERTING, M.D.
Saint Paul

IN discussing systemic manifestations of avitaminosis it must be borne in mind that while deficiency of a certain vitamin does produce more or less specific manifestations, the various vitamins have common functions, and inter-relationships do exist. However, for the purpose of this symposium, I will discuss the subject in relation to the individual vitamin.

Lack of vitamin A is chiefly concerned with xerophthalmic changes and night blindness, but animal experiment points to other interesting possibilities. It has been noted that vitamin A deficiency produces a marked susceptability to respiratory infections. Vitamin A seems to be a physiologic prophylactic against such infection by maintaining the integrity of the epithelial linings of the mucous tracts and skin. Once the infection has occurred, however, there is a good deal of difference of opinion as to the curative value of vitamin A therapy. Certainly no adequate proof has so far been submitted. The question of therapy is of particular interest to clinicians in relation to the so-called "common cold," but at the present time the prophylactic role must be given precedence. It has also been noted experimentally that vitamin A deficiency brings about a high incidence of renal calculi and a loss of the power of reproduction. Although these conditions may have their counterpart in man there is not sufficient evidence on which to recommend vitamin A therapy. Also certain types of secondary anemia are suspected of being associated with lack of vitamin A. It is well to call your attention to this fact in relation to prolonged regimes on poorly balanced diets such as are often used in cases of ulcer, nephritis and hypertension.

Lack of vitamin B, Bl or F is usually associated with neuritic changes. Extreme deficiency is characterized by multiple neuritis, edema, loss of appetite and cardiac weakness and this syndrome is pathognomonic of only one condition, beriberi. Beriberi is a disease of great antiquity and is endemic in the tropics and the orient where rice is the staple article of diet. The disease is unknown in America, except for imported cases. It should, however, be emphasized that ordinary neuritis is not a phenomenon of vitamin deficiency. Moderate deficiency of vitamin Bl gives a rather confused picture but the one outstanding symptom is anorexia. This symptom of loss of appetite is worthy of our special consideration because it is a complication of many diseases and its occurrence is often unrealized. These cases in my experience give the most gratifying results upon receiving a liberal supply of vitamin B. Growth and lactation are also very dependent on an adequate supply of this vitamin. Attention should be called to the observation of bradicardia developing in rats on a diet low in vitamin B and also the effects on the central nervous system, as is shown by the diminished maize learning ability of the rat.

Vitamin C apparently maintains the integrity of the vascular endothelium and is necessary for tooth formation and bone metabolism. Severe deficiency of vitamin C results in the classical picture of scurvy. Scurvy is one of the earliest known deficiency diseases. Hippocrates refers to it. It was prevalent among the Crusaders in the 13th century and history is filled with accounts of its devastating effects when groups of people were subjected to a rather strictly limited food supply. From the time of Hippocrates until as late as 1830 it was generally believed that all the animal and vegetable products which serve as food contained the so-called universal aliment. It is interesting to note that in 1795 the British navy allowed a ration of lemon juice to all sailors and the incidence of scurvy decreased immediately, but the merchant marine did not adopt the ration until 1865 and continued to have a large incidence of scurvy. In 1883 it was established that adult and infantile scurvy were the same entity, but it was not until the work of Holst and Froelich in 1907 that scurvy was definitely attributed to an accessory food factor.

Scurvy presents two fundamental types of lesions: (1) localized hemorrhage; (2) fragility of the bones. The condition is the result of a deficiency of the cementing substance between

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the endolethial cells and the blood vessels are weakened. Blood escapes into the various tissues and cavities producing hematomas of varying degrees everywhere. The gums become ulcerated and the teeth loosen in their sockets. The long bones fracture and form large calluses. Sub-periosteal hemorrhage is common, especially in the distal end of the femur and tibia. There is a deficient production of organic matrix so that mineralization cannot occur. The diagnostic criteria are as follows: (1) sallow skin (changes in complexion); (2) easy fatigue; (3) breathlessness; (4) pain in the joints often attributed to rheumatism; (5) hemorrhagic spots or large eccymoses especially in the extremities where bruises occur; (6) puffy, hemorrhagic and ulcerated gums. Complications such as pneumonia and enteritis are serious and account for nearly all the deaths.

Although scurvy is uncommon in America, except in artificially fed infants, the report of one case from the literature will emphasize the fact that the early symptoms are often obscure and that many early cases are being overlooked. The case is that of an adult suffering from duodenal ulcer who had been placed on the usual restricted diet plus alkali and who during the course of his treatment developed arthritis with purpuric spots. The case was variously diagnosed "rheumatism," "arthritis with pyorrhea" (all teeth were removed), and "rheumatism with purpura," before it was realized that the case was one of scurvy. Proper attention to the vitamin content of the diet was undertaken and the patient promptly recovered from his rheumatism.

Vitamin E is one of the least known of the vitamins, but experiments have shown that vitamin E deficiency results in sterility and if the deficiency is allowed to become extreme, the sterility is permanent. These facts have not been investigated in relation to man.

There are two conditions that are often considered manifestations of vitamin deficiency. The first is non-tropical sprue. A case is reported from the South where favorable results were attributed to intensive vitamin B therapy. This patient, however, was also on a special balanced diet and this was probably the only factor in the reported cure. Th. E. Hess Thaysen of Copenhagen in his latest book, *"Non-Tropical Sprue,"* just off the press, reviews the whole subject of non-tropical sprue and states that there is no proof that vitamins are a primary factor in this disease and he is of the opinion that there is no specific therapy. He gives in detail five specific diets and advises the trial of all if necessary. The second condition, nutritional edema or "war dropsy," has been suspected of being a vitamin deficiency disease, but the consensus of opinion at the present time is that it is due to a diet containing insufficient protein and an excess of fluids and salts. Treatment of these cases with high vitamin diet has not been successful.

SUMMARY

1. In my experience and in the experience of others avitaminosis is very rare in Minnesota. There does not appear to be any increase because of the present economic conditions.

2. Vitamin A is undoubtedly a prophylactic against respiratory infections but its curative value after the infection is acquired is very doubtful.

3. Prolonged use of milk and restricted diets as in the treatment of ulcer, nephritis and hypertension is prone to produce rather severe anemias that can be avoided by proper attention to the vitamin content of the diets.

4. Moderate vitamin B deficiency has one outstanding symptom: anorexia. All patients with loss of appetite should be given an adequate vitamin B intake. The results are often gratifying.

5. Many early cases of scurvy are being overlooked and it is well to remember that atypical arthritis and purpura, especially in those on a restricted diet, may be a mild scurvy.

6. Non-tropical sprue and nutritional edema, or "war dropsy," are not vitamin deficiency diseases.

TREATMENT OF MALNUTRITION IN ADULTS*

MOSES BARRON, M.D.
Minneapolis

THERE is a large and important group suffering from semi-invalidism composed of individuals who have no demonstrable organic lesions other than a chronic state of undernourishment. These asthenic patients, in addition to manifesting symptoms of weakness, easy fatiguability, nervous depression, a lack of stamina, indefinite gastric symptoms often associated with visceroptosis, show a marked inability to gain in weight. They are chronically tired, and seem to lack the feeling of well-being, a condition so essential to good health.

In spite of the large incidence of such cases there is a surprising lack of attention paid to them by writers of textbooks and articles in medical literature dealing with the general and dietary treatment of diseases. Careful and complete discussions are given of the dietary management of the various diseases with great elaboration of the treatment of obesity, but very little is written on the subject of constitutional malnutrition. Very likely Dame Fashion determines to a great extent the disparity between the emphasis given to reducing people and that given to increasing the patient's weight. From the health standpoint there can be no doubt that the undernourished present an even more important problem than the obese.

The difficulty in the past has been that no matter what treatment was instituted it was often impossible to increase the weight of many of these undernourished individuals. The Weir Mitchell method helps many, especially for the relief of the nervous exhaustion, but this method is too difficult and too expensive for most patients, since it involves a residence of from six to eight weeks in a hospital under the care and supervision of trained nurses. And even under this classical management many patients fail to gain in weight or gain very little. Many others are put to bed in their homes and are treated with high caloric diets, plenty of rest, and tonics and sedatives, but as often as not there is no increase in weight.

The discovery of insulin has brought about a marked change in the management of undernourished patients. Many observers began to notice the rapid gain in the insulin-treated diabetics. The gaunt, emaciated, skeleton-like patient of the pre-insulin era was being replaced by a well nourished, at times even overnourished, individual. This change in appearance and general well-being of the insulin-treated diabetic patient suggested the use of insulin in nondiabetic undernourishment.

REVIEW OF LITERATURE

Within a year or two after the discovery of insulin favorable reports of its use in the treatment of undernourished children began to appear in the literature (Pitfield,[25] Marriott,[19] Barbour,[2] Fischer and Rogatz[11]). About this time (1925) there began appearing in the German literature reports of the excellent results obtained also in adults through what they called the insulin Mastkur. Falta[8] was the first to report beneficial results in his first cases treated. He used increasing dosage up to sixty units daily and in a few cases up to 100 units daily. In a later report[9] he claimed good results in asthenic patients, in liver disease, in postoperative emaciation, and in nondiabetic acidosis, especially of dehydrated patients. The patients developed a hunger drive through its use,—"Heiszhunger." Bauer and Nyiri[4] substantiated Falta's findings. Since that time a voluminous literature has sprung up relative to the use of insulin in nondiabetic undernourishment, at first only in the European literature but in recent years also in the American literature. Favorable results have been reported for its use not only in constitutional undernourishment but also for the undernourishment associated with a large variety of diseases. Lepine and Parturier,[17] and Lawrence[16] have reported favorable results in cases of hyperthyroidism. Hofhauser und Schön[15] and Morin and Bouessee[21] find insulin valuable in the treatment of incipient tuberculosis as well as in slow clinically progressive tuberculosis with undernourishment. The improvement in the appetite together with the resultant gain in weight greatly favor, they believe, the increase in the resistance to the dis-

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ease. Heaton[14] found that this method of treatment was of real value in chronic tuberculosis and quotes many authors to prove that the insulin treatment of undernourishment both in childhood and in the adult has become a well established therapeutic procedure. Thalheimer,[29] and Fisher and Snell[12] report good results in pre- and postoperative nondiabetic acidosis. Vogt[30] has reported his results in over 100 cases treated with insulin and so enthusiastic is he about this method that he believes it will supersede all other methods in the treatment of undernourishment. Frank[13] has treated ambulatory patients with similarly good results. Schellong and Hufschmid[27] noted the development of a hunger-drive together with increase in pancreatic secretion following injection of insulin. Wiechmann[31] feels that insulin is almost as valuable in non-diabetic conditions as in diabetic. Among the American authors may be mentioned Blotner,[5] Barker,[3] Nichol,[22] Metz,[20] Fancher,[10] and Short,[28] who report excellent results from the use of insulin and state that the insulin sharpens the appetite, increases the feeling of well-being and increases the weight and strength of the individual. Even those who do not gain in weight seem to feel a definite tonic effect from insulin. Nichol[22] found that many of the patients kept their weight for many years, but most of them for a period of about three to six months. Eighty per cent of his cases showed an immediate gain in weight. Appel et al[1] report good results in the treatment of thirty-one undernourished psychotic patients. These patients had failed to gain in weight under the usual management but after the addition of insulin, from forty-five to sixty units daily, there was an apparent improvement mentally as well as physically.

A great deal of work has recently been done to explain the manner in which insulin brings about these favorable results. It has been found that the effect of insulin on metabolism is far from a simple one. It does more than merely influence the utilization of the carbohydrates and fats within the body: Lueders and Watson,[18] after a careful study of eighteen asthenic undernourished patients with gastric symptoms found that insulin produces a heightened potency of the pancreatic enzymes, a greater secretion of bile and consequently a more complete digestion, absorption and assimilation of food. All of the patients gained in weight on the rich carbohydrate and fat diet with the aid of twenty units of insulin three times a day. Quigley[26] found that insulin causes a definite increase in gastric motility and tonicity accompanied by a prolonged hunger period. This effect is quickly inhibited by the introduction of sugar in the duodenum or by a subcutaneous injection of adrenalin or atropine. Bulatao and Carlson[7] also found that experimental hyperglycemia inhibits the normal gastric hunger contractions while insulin hypoglycemia increases the stomach tonicity and contractions. Okada et al[23, 24] have found that glucose by stomach or intravenously inhibits the secretory center of gastric, pancreatic and biliary juices, while hypoglycemia on the other hand accelerates it. It is not the insulin which acts directly to bring about these effects, but it is the resultant dextrose deficiency which evokes a stimulation of the secretory centers and thence through the autonomic nervous system the stimulus is carried to the active tissue cells. These observations help explain how the introduction of glucose into the stomach or intravenously produces a feeling of fullness and loss of appetite, as is the case for instance when a child loses its appetite from eating candy and sweets, for the presence of an increased amount of sugar in the blood inhibits the gastric, pancreatic and biliary motor and secretory functions.

PERSONAL EXPERIENCE

I have been interested in the use of insulin for the treatment of malnutrition since 1926 when I first saw Falta and Bauer administer it for the treatment of leanness. Since then I have used it for the specific treatment of undernourishment in a large number of cases of which thirty-two are listed in Chart I. In addition I have outlined my method of insulin treatment to a number of physicians who have reported very satisfactory results from its use.

Method of Treatment.—Most of my patients are hospitalized and a few of them carry out the treatment at home, while continuing their usual duties. In the hospital the patients are at first kept in bed and later are given bathroom privileges and finally are allowed to increase slowly the time of sitting up and the distances they walk. From the beginning they are placed on a concentrated high caloric diet of about 3,500 to 4,000 calories divided into three main meals and three lunches. The increase in diet is principally in

CHART I

Case No.	Sex	Age	Duration of Illness	Weight at Onset	Gain	No. of Days Treated	Insulin Dosage, Units	Condition on Discharge
1	F	28	1 yr.	90	11.5	32	20–15–20	Much improved.
2	F	40	12 yrs.	100.5	9	16	20–0–15	Much improved.
3	F	30	10 yrs.	60	4	12	20–20–20	Slight improvement. Little coöperation.
4	F	21	5 yrs.	104	6	12	20–15–20	Definite improvement.
5	F	68	1 yr.	99	19	39	15–15–15	Excellent results. Wt. 1 yr. later 136. Wt. 6 yrs. later 145.
6	M	31	3 mo.	115	9.5	16	20–20–20	Much improved.
7	F	27	8 mo.	101	3	17	20–15–20	Slight improvement. Severe headaches.
8	F	60	6 mo.	82	6	21	20–10–15	No improvement. Severe depression. Melancholia.
9	F	65	1 yr.	101	2 (loss)	43	20–20–20	No improvement. Melancholia. Tube-fed.
10	F	32	1 mo.	87	12	14	20–20–15	Greatly improved. 8 mo. later, 121, gain of 34 pounds.
11	F	16	1 mo.		some	17	20–15–15	Bedridden. Severe neurosis. No cooperation.
12	F	20	2 yrs.	92	13	33	20–0–20	Treatment continued at home. Wt. 2 mo. later 118. Felt well.
13 & 14 (Twins)	F	22	10 yrs.	94	11	20	25–20–20	Much improved. Wt. 4 mos. later 116.
	F	22	10 yrs.	91	11.5	20	25–20–20	Much improved. Wt. 3 mos. later 112.
15	F	31	1 yr.	106	15	83	25–25–20	Greatly improved. Well 1 yr. later, wt. 132.
16	F	22	2 yrs.	88	11	26	20–15–15	Much improved.
17	F	31	15 yrs.	120	12	30	25–20–20	Improved every way. Wt. 6 wks. later 136.
18	F	53	1.5	125	5	13	25–25–20	Some improvement.
19	F	40	1.5	109	19	30	25–25–20	Marked improvement on ambulatory treat.
20	M	20	2 yrs.	119	6	23	30–30–25	Little improvement. Better later.
21	F	20	5 yrs.	86	7.5	21	25–25–20	Marked improvement.
22	F	28	5 yrs.	102	16	41	30–30–25	Marked improvement.
23	F	53	10 yrs.	74	15.5	36	30–25–20	Improved but weak. 5 mos. later wt. fell to 81
24	F	36	6 mos.	102	1	43	30–25–25	Psychoneurosis. Improvement hindered by operation on tooth.
25	F	37	1 yr.	100	10	24	25–20–25	Marked improvement. Insulin continued at home. Wt. 1 mo. later, 115.
26	F	40	6 mos.	90	22	52	30–25–25	Marked improvement. No gain 3 mos. prev.
27	F	32	6 mos.	111	8	10	30–25–25	Definitely better.
28	F	21	6 mos.	110	14	21	20–20–20	Much improved. Ambulatory treatment.
29	F	67	2 yrs.	95	31	67	30–25–20	Very marked improvement.
30 (23)	F	54	10 yrs.	69	16	47	25–20–20	More marked improvement than 1 yr. prev. (23).
31	F	50	8 yrs.	99	19	40	20–20–20	Definite improvement.
32	F	27	4 yrs.	95	22	50	25–25–25	Excellent results. Ambulatory treatment.

carbohydrates and fats. The rationale of the treatment is carefully explained to the patients so that they may coöperate in preventing the occurrence of insulin reactions. A very detailed explanation is given as to how hypoglycemic reactions may result from an insufficient amount of food taken. The symptoms of a reaction are described to them in detail as a sense of restlessness, anxiety, blurring of the vision, palpitation, sweating, hot flushes, a stiffening and numbness of the tongue and lips, tremors, chills, diplopia, weakness in the legs. It is always carefully emphasized that none of these symptoms prove serious, and that they are entirely avoidable through the ingestion of sufficient amounts of nourishment. During the course of treatment they are ordered to have within reach constantly some form of concentrated carbohydrate such as sugar, candy, sweet chocolate or sweetened orange juice. They are instructed to take some of this at the slightest suggestion of the onset of any of the above mentioned symptoms. In the hospital a glass of orange juice sweetened with about six teaspoons of sugar is usually placed at the bedside every morning before the first injection of insulin and is kept there unless needed during the day until bedtime, when they are advised to drink it. As aforementioned, the diet consists mainly of carbohydrates and fats and contains large amounts of such foods as cereals, cream, butter, fat meat, bacon, potatoes with gravy, bread, malted milk and milk enriched with cream. Whenever possible a small bar of sweet chocolate is taken at the end of the meal.

The insulin is injected from twenty to thirty minutes before each meal. The first injection is five units three times a day with subsequent increase of one to two units three times a day until twenty or at times twenty-five units three times a day is given. In a few selected cases as much as thirty-five units three times a day is administered often without any hypoglycemic reactions. One must constantly be on the lookout not to inject a large dose of insulin when the patient is indisposed to eat the usual meal or is suffering from nausea and vomiting. If there is no vomiting the insulin can always be buffered by sufficient amounts of well sweetened orange juice by mouth. In cases of vomiting as much as 250 c.c. of 20 per cent glucose may be given intravenously and this will promptly obviate any hypoglycemic manifestations. I have never had to resort to this emergency measure.

In conjunction with the use of insulin I always prescribe a bitter tonic containing a large dose of nux vomica and also bitter cascara when necessary for the bowels. Since many of these patients are neurotic I administer a sedative mixture after meals and at bedtime. Proper relaxation is an essential part of the treatment. The patients are exhorted to be calm and cheerful and it is made clear to them that their being so greatly facilitates the gaining in weight.

Results of Treatment.—Chart I shows a résumé of the results obtained in the treatment of a series of thirty-two patients. In this group all but two were females and all but one were over twenty years old. Twelve patients were between twenty and twenty-nine, eight between thirty and thirty-nine, three between forty and forty-nine, four between fifty and fifty-nine, four between sixty and seventy. The average dosage administered was seventy units daily, in a few cases from eighty to ninety units were used. I have found that some patients will respond to large doses only, and in general the larger doses bring about the more rapid improvement. In the literature some observers have obtained good results with only thirty units daily. I have always found that the improvement increases with the increase in the dosage, of course always within physiological limits. Four of the thirty-two patients showed no improvement for obvious reasons and in four others the improvement was only slight. In Case 3 there was no coöperation from the patient and the treatment had to be discontinued. In Case 7 there was at first some improvement but severe migraine headaches interfered with further progress. Cases 8 and 9 were old women suffering from severe melancholia, the latter had to be tube-fed during her entire stay in the hospital. Case 11 was an unfortunate case of a despondent girl suffering from the effect of pronounced scoliosis which had resulted from a severe attack of infantile paralysis. She developed a severe case of self-pity and could not be made to coöperate. Case 24 began to improve but an operation performed on an impacted tooth brought on a severe depression that impeded further progress. The twenty-four remaining patients showed a very definite improvement so that 75 per cent of this series improved physically and mentally and in a rela-

tively short period of time. Nineteen of these twenty-four patients gained more than ten pounds in weight during short courses of treatment and many of them continued to gain after the insulin injections were stopped. The greatest gain was in Case 29 where the patient increased thirty-one pounds in sixty-seven days. A woman sixty-eight years old (Case 5) was sent in with a diagnosis of a terminal state of malignancy, she was extremely emaciated, completely exhausted and had been bedridden for some time. Since no organic lesions were demonstrated by careful examination she was placed on the insulin regimen on which she gained nineteen pounds in thirty-nine days. When seen one year later she weighed 136 pounds, a total gain of thirty-seven pounds, and six years later, that is, April 24, 1933, she was in excellent health and spirits and weighed 145 pounds, a gain of forty-six pounds over her original weight. Case 19 is a nun who had been treated for a year with rest and forced feeding and a change of environment with practically no improvement. Her weight ranged between 103 and 109 pounds. When she returned to work as an x-ray technician in a hospital she still felt tired and exhausted. She was now placed on the ambulatory management with insulin. Within a month she gained nineteen pounds and she has retained practically all her weight and the sense of well being during the past four years. Several patients have found that they either have to use insulin continuously or repeat the course of treatment occasionally in order to retain their weight and strength and keep in condition to continue with their work. Some of the patients experience a general tonic effect which is often greater than would be indicated by the gain in weight alone. Cases 13 and 14 are twin sisters who suffered from chronic under-nourishment. Both were placed on the same routine management at the same time and both responded equally well, almost identically. Case 28 is a nurse who felt tired and rundown most of the time. She gained fourteen pounds in twenty-one days under the ambulatory treatment. She continued to gain in weight and in general well-being, and when last seen, on May 10, 1933, two years after treatment, she weighed 130 pounds and was feeling perfectly well. Case 32 is a teacher who had tried different methods for gaining in weight without success until she was placed on the insulin ambulatory management. Within a relatively short period of time she gained twenty-two pounds in weight and felt better and stronger than she had felt for many years.

The main symptoms complained of by this group of patients were weakness, depression, frequent crying spells, nervousness, trembling, palpitation, insomnia, at times nausea, vomiting and diarrhea, and always an inability to gain in weight. Following treatment the patients seem to acquire a greater sense of well-being, a more cheerful outlook on life, an improved disposition and in a general way they appear better. In some cases unfortunately the improvement is only temporary but in a large number it seems to be quite permanent.

Mechanism of Effect.—The general improvement in most of the patients treated, psychological as well as physical, shows that there is a profound constitutional effect produced by the administration of insulin. Many explanations are offered for the beneficial effect, especially for the increase in appetite and the resultant gain in weight. Quigley and Carlson have shown that there is a rise in the gastric tonus with repeated rapid contractions and prolonged hunger contractions as a result of the injections of insulin. In some patients there develops a ravishing appetite, Falta's "Heiszhunger." It has been shown that the insulin hypoglycemia produces a stimulation of the secretory centers of the pancreas, stomach and biliary system. There is an improvement in the carbohydrate metabolism as well as in the general metabolism with increased digestion, absorption and assimilation of the food ingested. There is probably also a greater permeability of the tissue cells for sugar with increased oxidation and greater glycogen deposit, as well as some increase in cellular water retention. The increase in hunger from the prolonged hunger contractions of the stomach together with the increase in the secretion of the gastrointestinal juices and the increased secretion from the biliary system as well as the better utilization of the carbohydrates and fats through the direct specific action of the insulin, help to explain the favorable results in the insulin treatment of undernourishment.

PREVENTION OF UNDERNOURISHMENT

It may not be amiss at this time to say a few words in regard to the prevention of certain

forms of undernourishment. There is a form of malnutrition which is induced by too restricted diet and for too long periods of time in the treatment of various ailments. The seriousness of such malnutrition is too often overlooked by many doctors. In addition to the nourishment resulting from such dietary restrictions there is often associated certain forms of avitaminoses which in themselves are responsible for serious disease states. Usually the average American diet is adequate to prevent the development of deficiency diseases but the restricted diets are often lacking in sufficient amounts of certain vitamins. In a personal communication to me Dr. Walter Alvarez stated that most of the patients he has seen with symptoms of avitaminosis had been suffering from too restricted diets imposed by doctors for too long periods of time in the treatment of certain diseases like nephritis, ulcer, hypertension, et cetera.

Many doctors still impose stringent low protein diets in the treatment of hypertention, eliminating meats, fish, cheese, eggs and other protein foods. Careful observations have established the fact that there is no rational basis for such restriction. A moderate amount of protein food has been found to have no unfavorable effect on the blood pressure.

In the treatment of chronic peptic ulcer and especially chronic ulcerative colitis, undernourishment and deficiency states have been developed from too limited diets. In diarrheas, especially, the nourishment is interfered with by the improper absorption and elimination of the food ingested. Xerophthalmia and less easily recognized deficiency states may often result. It might be well to recall Brown's[6] suggestion that "far more harm is done by diets too limited than by one too free."

Another group of patients that often suffers from too strenuously restricted diet is that of chronic Bright's disease. It is too generally assumed that whenever albuminuria is present the patient has to be placed on a rigid protein restricted diet. This is quite improper management since it has been found that the protein restriction need be little or not at all unless there is already definite evidence of renal insufficiency with beginning accumulation of metabolities in the blood. Indeed, certain types of Bright's disease which have a strong nephrotic element are often benefited by high protein diets. It is also to be noted that the kind of protein used whether from red meat, white meat or from other sources, is absolutely of no importance. Anemias as well as undernourishment may result early from too rigid dietary restrictions.

The same holds true in the albuminurias of congestive heart failure. Here also no dietary restrictions are necessary other than the restriction of salt and water for the prevention of edema, and the avoidance of too large or heavy meals at one time so as not to embarrass the heart's action. No protein restriction is necessary.

Dietary restrictions for obesity are often too drastic. Deficiency states involving severe exhaustion and nervousness occasionally follow. In some patients the losing in weight continues after the desired stage has been reached, often associated with increasing nervousness. It is usually advisable to give brewer's yeast, cod liver oil, fruits and vegetables in large amounts to compensate for the restriction of food necessary to lower the calory intake. In diseases of the joints various fads of dietary management have been used which may lead to undernourishment of the patient. It is now generally agreed that the full caloric anti-constipation diet, with the addition of some vitamines, is best in all cases of chronic infectious arthritis where there is no marked overweight.

There is usually altogether too great restriction of diet in post-operative cases where there has been found some associated condition as a mild nephritis, hypertension, heart condition or moderate grade of albuminuria from whatever cause. Unless there be some definite surgical indication for the restricted diet the choice of food as far as the associated condition is concerned may be very liberal. There is little danger, as a rule, of a recent postoperative patient overeating any certain kind of food. Restriction in protein is very seldom necessary. The patient should be allowed considerable freedom of choice since it is necessary usually to cater to the whimsical appetite of the postoperative patient.

In addition, may I say that not only should the treatment be directed so as to avoid as much as possible, disturbances of malnutrition, but that as a general rule no undue restrictions or hardships should be placed on patients, and under all

circumstances the regimen should approach the normal as nearly as possible.

SUMMARY AND CONCLUSIONS

1. Insulin is a valuable aid in the treatment of undernourishment, both diabetic and non-diabetic. Its life-saving usefulness in diabetes is well known to all.

2. Undernourishment of various degrees and often of unknown origin is frequently encountered by all practitioners of medicine. Patients affected by such undernourishment frequently present a group of symptoms which seem to be directly related to the undernourished state. Improvement in nourishment usually promotes the general well-being of the patient.

3. Many undernourished patients who do not respond to the usual management of rest, tonic, and high caloric diet, will show definite improvement after the addition of insulin. The beneficial results are obtained more rapidly.

4. In addition to the specific and indirect effects of insulin on appetite and metabolism, the fear of insulin reactions hangs over the heads of the patients like the sword of Damocles, inducing them to ingest much more food.

5. The insulin fattening cure is simple to carry out if properly understood. Careless administration without proper attention to the balancing of the diet, may of course, lead to uncomfortable reactions. The results from the ambulatory method seem to be just as good as in the hospitalized cases. This makes this method especially valuable, since more patients may enjoy its benefits.

6. The easy accessibility to carbohydrates such as sugar, candy, or sweet drinks during the course of treatment is very essential.

7. In the series of thirty-two cases treated with insulin, here reported, there was a satisfactory improvement in 75 per cent of the cases. In most of the cases the improvement was more rapid and more pronounced than that obtained with non-insulin methods.

8. More attention should be paid to the danger of too rigid dietary restrictions in the treatment of various ailments, especially those where diet is thought to be an important factor. Many cases of undernourishment and deficiency states result from too drastic diets continued over too long periods of time.

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VITAMIN DEFICIENCY IN CHILDHOOD*

P. C. Jeans, M.D.
Iowa City, Iowa

IN this symposium the part played by vitamins in nutrition and the various manifestations of vitamin deficiency already have been reviewed. There remain to be discussed, in this presentation, certain applications of our present knowledge of the vitamins as it concerns children. To this end the subject is best approached by considering the vitamins individually.

The pathological picture produced by vitamin A deficiency includes changes in the epithelium of the nose and throat which make these areas more susceptible to secondary invasion by bacteria. Thus, vitamin A deficiency can become a predisposing cause of upper respiratory infection and sinus disease. When a patient comes under care with a history of frequently recurring upper respiratory infection, it is desirable to be certain that a sufficient amount of vitamin A is being ingested. In order to attain this certainty, often cod liver oil is prescribed. At the same time one should not be too greatly disappointed if this therapy fails to accomplish a decrease in the amount or frequency of infection. Upper respiratory infections occur from other causes than vitamin A deficiency. This is especially true of such specific infections as the common cold. Few would expect to create a specific immunity by nutritional means. Yet our current literature contains a number of reports of failure to reduce the frequency of the common cold by cod liver oil administration, and these reports carry the inference, at least, that vitamin A is of little value as an anti-infective agent. It is desirable to recognize the fact that vitamin A deficiency may lead to respiratory infections, but at the same time it is necessary to keep oriented to the extent that we do not deprecate the usefulness of vitamin A because it fails us in instances in which we really should not have expected success.

Vitamin A deficiency of sufficient degree to produce the well known and outspoken symptoms characteristic of this deficiency is rare in this country. We have no good idea of the prevalence of a moderate deficiency of this vitamin. In searching for a clinical measure of moderate vitamin A deficiency it occurred to us that night blindness might serve such a purpose. By means of a photometer we have determined the speed of recovery of acuity of vision after exposure to a bright light. We have found that approximately 20 per cent of the children applying to our children's hospital for treatment have a loss of visual acuity in the dark, and that the acuity of vision can be restored by cod liver oil administration. We believe that we have established the validity of this procedure as a method of deter-

*From the Department of Pediatrics, College of Medicine, State University of Iowa. Read before the annual meeting of the Minnesota State Medical Association, Rochester, Minnesota, May 23, 1933.

mining vitamin A deficiency. We would attach no special significance to the incidence figures we have obtained up to now, except possibly that they permit us to state that in this particular class of children, moderate deficiency of vitamin A is relatively common. From this finding we would not draw the inference that vitamin A concentrates are indicated routinely in the everyday feeding of children. It is our opinion that a good diet will supply an adequate amount of vitamin A, and that, ordinarily, the use of a good diet is the better method of obtaining this vitamin.

Animal experiments in our own clinic and elsewhere have shown that ingested mineral oil carries away, in the feces, some of the vitamin A of the food. When the amount of vitamin A permitted to the animals is only sufficient to meet the minimal requirements for growth, the addition of mineral oil to the diet in amounts proportionate to the usual human dose causes the animals to die with signs and symptoms of vitamin A deficiency. When the animal receives larger amounts of vitamin A, mineral oil does not have this effect. We encounter few opportunities to determine the application of this experimental finding to the human. Recently, a child with loss of visual acuity in the dark failed to recover normal acuity of vision after the administration of cod liver oil for several months. She had been taking a generous dose of mineral oil daily. Her vision became normal very soon after the administration of mineral oil was discontinued. It seems entirely possible that ingestion of mineral oil may be a contributing factor in vitamin A deficiency in the human.

In discussing vitamin B, I shall include those factors which make up what is known as vitamin B complex. Vitamin B preparations are extensively advertised. The question arises as to the general need for such preparations and as to the prevalence of vitamin B deficiency. The prevalence of this disorder is difficult to determine. We have no definite measure of moderate degrees of vitamin B deficiency. As judged by the content of the average American diet, vitamin B may readily be moderately deficient in the diet of a considerable number of people. The published reports of clinical observations are not conclusive in this respect. The improvement reported in some of the feeding experiments may have been due to factors other than the vitamin B content of the dietary additions. It is definite that vitamin B deficiency causes loss of appetite. However, if vitamin B addition to the diet is the only change made in the regime of the child with poor appetite, the chances are great that no improvement in the appetite will be noted. Poor appetite in the child is dependent upon psychic factors and feeding habits in a high proportion of cases. If vitamin B deficiency is present in addition, it is difficult to detect. It is true, also, that vitamin B deficiency causes atonic changes in the intestinal tract which may lead to constipation. Despite this fact, one rarely encounters a child whose constipation is relieved by the addition of vitamin B to the diet. In evaluating this statement it is necessary to realize that wheat germ preparations have laxative effects which are entirely independent of their vitamin B content. The relief of constipation by wheat germ is not evidence of a preceding vitamin B deficiency, despite many advertising inferences to the contrary. Whether or not a moderate degree of vitamin B deficiency is common, it seems definite and well established that a good, well balanced diet of common, natural foods supplies an adequate amount of vitamin B for growth and health, and, consequently, no need exists for special vitamin B preparations for everyday use by the normal individual when proper thought is given to the diet. In so far as this contention can be demonstrated by the usual clinical means, it has been shown in groups of infants and children which we have had under special nutritional observation. These individuals have grown at a rate considerably exceeding the average, have had excellent appetite and robust health, and have been lacking in all of the symptoms which are attributed to vitamin B deficiency; yet they received only a good diet with no special vitamin B preparation.

Scurvy, developed to the extent that it is recognized, has become a rare disease in this country. In our practice we almost never see a case at the present time. A statement that vitamin C deficiency is uncommon is easily credible. Yet we have no accurate knowledge of the extent of moderate and unrecognized degrees of such a deficiency. Göthlin, by means of a tourniquet-capillary permeability test has found subclinical vitamin C deficiency to be relatively common among the children of northern Sweden during the winter season. Such a finding would not

necessarily hold for this country, yet we have no secure basis for optimism in this respect. It is entirely possible, were a delicate test applied, that a wholly unsuspected incidence of this condition would be found. However, any apprehensions in this respect would be put quickly at rest by the application of a more wide-spread knowledge of what should constitute a normal diet. In considering the requirements of a normal diet, the inclusion of such recommended quantities of orange juice as a quart a day seems ridiculous.

Of all of the known vitamins, vitamin D is the one of which we have most reason to fear a common deficiency. This fact is so generally known that it has become common practice to include some good source of vitamin D in the diet, especially at the age when the clinical effects of a deficiency are so obviously manifest. Though rickets is far less common than formerly, it is still to be observed with much too great a frequency. By inference it would seem that Nature intended that we obtain much of our vitamin D through the medium of sunshine; the distribution in our common foods is relatively meager. The practice of intentionally including in the diet some special source of vitamin D is an excellent one. In infancy such a practice serves to prevent rickets, while in the older child it serves as an additional safeguard in meeting an unknown requirement with a sparse content in the food.

Rickets in infancy probably is not as frequent as some of the statistical reports might lead us to believe. Reports, which state that approximately 80 per cent or more of the babies in the temperate zone have rickets in spite of cod liver oil therapy, are based upon Roentgen-ray studies. Roentgenologic criteria for the diagnosis of mild rickets need revision. This statement is based in part on a study of a carefully observed and closely supervised group of babies which we have had under observation. These babies received an abundance of food, with the result that they grew at a rate more rapid than the accepted standards. The increased growth was in height as well as in weight. That the increased growth was of good quality was attested by the large daily retentions of nitrogen, calcium and phosphorus, and by the physical vigor of the infants. Roentgenograms were taken at monthly intervals. These were reviewed by expert roentgenologists in two different localities. These men were in agreement in the opinion that at some stage in their development practically all of the babies presented evidences of rickets according to current criteria. Our belief that these babies did not have rickets is based upon facts which seem sufficiently significant.

A good indication that the roentgenograms did not show very definite evidences of rickets is that they were classed as negative for rickets by an orthopedic surgeon well accustomed to the interpretation of bone roentgenograms, and also by an internationally known anthropologist who has studied such pictures for many years. In these babies growth and calcification were taking place at an unusual rate. The increased rate of calcification was demonstrated by the appearance of carpal bone shadows in the roentgenograms considerably in advance of the expected or average age. In rickets one expects a decreased rate of calcification. The retentions of calcium and phosphorus were greatly in excess of the accepted average standards, whereas in rickets a decreased retention is expected. At all times the blood calcium and phosphorus were found to be at high normal levels. Finally, some of these infants were diagnosed as having rickets in middle and late summer, despite the fact that the babies had spent much of the day time out of doors. In view of all of these considerations we believe that such changes as were observed in the bones of this group of babies were entirely normal for rapidly growing bone. It is on the basis of such reasoning that we question the reported high incidence of rickets among babies who are receiving good nutritional supervision. The reported incidence of rickets, therefore, does not serve as an index of the prevalence of vitamin D deficiency.

It is of interest, also, that the babies just discussed received routinely only one teaspoonful of cod liver oil daily in addition to their regular diet which contained no other special source of vitamin D. If it may be granted that the babies did not have rickets, then it may be concluded that one teaspoonful of cod liver oil daily is sufficient to prevent rickets in the locality in which these observations were made (Iowa). This finding is not necessarily a contradiction to the recommendation of three teaspoonfuls of cod liver oil daily made by the Council on Pharmacy and Chemistry of the American Medical Association,

for the reason that this group, in expressing an official opinion desired to recommend a dose ample for the least favorable localities.

In dental caries we have a disease which has been proved to be dependent upon nutritional deficiency. The wide prevalence of this disorder seems an excellent index of the great extent of some type of nutritional deficiency in our population. Various observers have selected and emphasized some one or more of several different dietary factors as being of primary importance in the control of tooth decay. It is our belief that there is no single specific deficiency responsible for tooth decay, and that the individual nutritional factors should not receive undue emphasis. We should not design a diet specifically for the prevention or arrest of dental caries. Rather, it would seem preferable to prescribe a "complete" diet, which, because of its completeness, would not only accomplish our aims in regard to dental health, but at the same time would satisfy all of the many nutritional requirements. Even though we have this attitude in regard to the nutritional essentials responsible for dental health, we are quite ready to admit that vitamin D is one of the important factors. Mellanby has observed arrest of dental caries in some of a group of children when administration of viosterol was the only change made in the children's care. To what extent a deficiency of vitamin D is the chief or even an important factor in tooth decay among children in general we have no knowledge. In the present state of our knowledge it would seem preferable to insure an adequate supply of this material.

For obtaining vitamin D in addition to that found naturally in our food we have available an unusual number of methods. These include direct irradiation of the body with ultraviolet energy and the administration of cod liver oil and its concentrates and the administration of viosterol. They include also the use of foods which have been irradiated or to which vitamin D in some special form has been added directly or indirectly. By indirect addition I refer to the feeding of irradiated foods to the cow for the purpose of increasing the vitamin D content of the milk. The choice among these various methods is not easy and each may be employed advantageously, at times, for some special indication.

Despite this multiplicity of means for supplying vitamin D, we find vitamin D deficiency still rather widely prevalent. This is good evidence of a lack of application of such knowledge as we have, and is an indication that we should encourage some prophylactic measure that has a wide applicability and which requires little initiative on the part of the consumer. The increase of vitamin D in foods before distribution either by irradiation or by the addition of concentrates would seem a satisfactory answer to this problem. The iodine deficiency problem is partially met in a similar manner by the addition of iodine to salt. In making any such widespread prophylactic attempt, a decision must be made as to what food shall be the vehicle and as to what methods shall be used in enhancing the vitamin D value of those foods. This problem is not a simple one. The irradiation of a large number or variety of foods should not be permitted nor approved. Such a procedure would lead to too great a variation in dosage for the individual, with the possibility that certain individuals would be ingesting an excessive and, possibly, a harmful quantity. The indications are that we may now be headed in the direction of such a chaotic state.

Some food, which is universally used, should be employed as the medium for this dietary addition. Such a food is milk. Milk is the basic food in the diet of every infant, and it is the artificially fed baby who is most likely to develop rickets. Milk should be considered an essential inclusion in the diet of every growing child. If a suitable amount of vitamin D were added to all milk distributed by commercial dairies, a great amount of benefit would be obtained in the direction of general prophylaxis against vitamin D deficiency, even though such a method is not readily applicable to rural districts. This method of prophylaxis is relatively inexpensive and it is automatic; both of these are advantageous features.

Milk is an excellent medium for additional amounts of vitamin D not only because of its universal use, but also because it is our one best source of calcium and phosphorus. Other foods, as compared to milk, are relatively lacking in these essential minerals, especially in calcium. Vitamin D is concerned with the utilization of calcium and phosphorus and all three of these materials would be associated in vitamin D fortified milk.

Before we know exactly what we are doing

in the fortification of milk with vitamin D, much clinical research is necessary. Apparently the present methods of measuring the vitamin D content of foods in terms of rat units do not give us the type of information we need. According to the observations of A. Hess, equivalent antiricketic effects in the child are produced by 1 rat unit of vitamin D in irradiated milk, 4 units in cod liver oil and 8 units in viosterol. A statement of the vitamin D content of various antiricketic substances in terms of rat units is likely to give a false impression as to their antiricketic value for the infant. Apparently 50 rat units daily of vitamin D as contained in irradiated milk will prevent and cure rickets readily. In rat unitage this quantity is equivalent to one half teaspoonful daily of a high grade cod liver oil. In order to know the relative effects of different methods of milk fortification, and from this the amount of fortification desirable, it is necessary to be able to measure the vitamin D content of foods in terms of child units, rather than in rat units. Such information as we now have indicates that relatively small amounts of vitamin D, as contained in irradiated milk, are highly efficient as an antiricketic agent and, probably, as a consequence, little fear need be entertained concerning the danger of overdosage and harmful effects when the use of this procedure is properly controlled.

Vitamin E we shall mention only in passing. It would seem that this essential food material is so widely and generously distributed in foods that we scarcely need concern ourselves about its possible deficiency in the diet.

In this discussion, has been stressed the opinion that for routine management of the diet of children no indication exists for the use of special vitamin preparations, with the possible exception of preparations of vitamin D. It has been stated that we can obtain all of these nutritional essentials from common natural foods, and this should be the preferred method. A well-chosen diet of natural foods is nutritionally superior to a diet composed of concentrates. One very good reason why this is true is that, in all probability, essential nutritional factors exist which are still unknown to us. Evidence is developing that some nutritional factor particularly useful for growth and lactation is present in liver and that this factor is not any of the present known essentials. Other substances also will be included among the human requirements as our knowledge of nutrition increases. All of these are more likely to be included in a good mixed diet than in a diet of concentrates.

Nearly thirty years ago Hopkins pointed out this same general truth as follows: "The animal body is adjusted to live either upon plant tissues or the tissues of other animals, and these contain countless substances other than the proteins, carbohydrates and fats. Physiological evolution, I believe, has made some of these wellnigh as essential as are the basal constituents of the diet. . . . . it is certain that there are many minor factors in all diets of which the body takes account. . . . . I can do no more than hint at these matters, but I can assert that later developments of the science of dietetics will deal with factors highly complex and at present unknown."

In condemning concentrates for routine use, I may have conveyed the impression that I believe the average diet to be satisfactory as it is now constituted. I desire to correct any such impression. The evidence is abundant that the average diet at all economic levels is deficient. Excellent evidence for this lies in the prevalence of dental caries, which already has been discussed. When a disease, which is dependent upon nutritional deficiency, is found in 80 to 90 per cent of our children, the conclusion is obvious that the average person has little conception of what constitutes an adequate diet and that our present dietary habits are far from satisfactory.

DISCUSSION ON PAPERS OF DRS. G. O. BURR, S. E. SWEITZER, HARRY OERTING, AND MOSES BARRON

DR. W. C. ALVAREZ (Rochester): I feel a bit like the minister who was aked to discuss the immortality of the soul in five minutes. It is hard to sum up all this splendid symposium in ten minutes. I think you will agree with me that all of the speakers have been eminently sane, judicial and helpful. That is just what those of us who planned this meeting wanted. We hoped the speakers would sift out from the enormous amount of information obtained from work on rats, that which should be useful to us practicing physicians. We want to know how much we need to worry about these vitamins, when we must worry, and what symptoms we must watch for.

I concur heartily in what the speakers have said, and I have been delighted with their papers. I think they have all steered wisely between the Scylla of lack of interest in the remarkable work which has been done on animals in the last twenty or thirty years, and the Charybdis of being stampeded into foolish behavior, particularly by the literature of men who have something to sell.

Unfortunately, today the layman must get most of his impressions on this subject from men who are spending millions on full page advertisements in the *Saturday Evening Post* and other journals. These men will, of course, quote any scripture they can find to serve their purpose, which is to frighten people into buying their particular "health food." One cannot help wishing that these tremendously expensive and powerful campaigns of education might be directed by more judicious teachers.

Let me now summarize brifly the questions that have interested us most this morning.

First: How much of that which is being learned from experiments on rats is applicable to man, and particularly, to adult man?

As Dr Burr pointed out, vitamins are producers of growth, and hence we have to be most careful to supply them to the growing child, the pregnant woman, and the nursing mother. They who are building something must be supplied with all of the building blocks that are necessary to growth, and if we do not supply them every week they may get into trouble. I, an adult, am built. All I need is the fuel to keep me going and a certain small amount of nitrogen with which to repair the daily damage done to my tissues. If necessary, I can go for weeks and perhaps months without vitamins.

Second. How much of the several vitamins must children and adults get every day to remain in health? What are the basic requirements? I am glad that Dr. Jeans has given us some answer to this question. I feel sure that today many worried and well intentioned mothers must be giving their children a far greater dosage of vitamins than is necessary.

We need to know also if it does any good to stuff a child with far more vitamins than are necessary. May not enough be as good or better than a feast? May we not also injure our children by stuffing them with big doses of these exceedingly powerful substances? I have been somewhat reassured by noting that the dosages of Vitamin D that produce arteriosclerosis and death in animals are very large, but I have become worried again over the published reports of children dying with signs of injury due to an excessive intake of Vitamin D.

Next, what are the earliest signs of disease due to avitaminosis? Again, Dr. Jeans has helped us by showing that tests are now being designed which will help in demonstrating latent disease of this type.

Some of you who use high vitamin diets in many conditions may think, when your patients get better, that you must have treated an avitaminosis and cured it. But may you not have helped more by improving the general state of nutrition? It will take a long time and a great deal of good clinical observation before we know how much of the disease that we now seem to help with a high vitamin diet is really caused by lack of vitamins.

Another big problem is: How essential is it to supply some of the vitamins to adults? For instance, is Vitamin D at all necessary to adults and especially to an adult who lives on a generous diet and who gets out in the sun? Recent studies by Hess seem now to have knocked out what few props there were under all the ballyhoo about vitamins being necessary to protect us from respiratory infections.

We have been given here today some idea of how common or how rare avitaminosis is in the practice of American physicians. Most of the speakers who have studied the conditions here in Minnesota have told you that except for rickets, such diseases appear to be very rare. Rickets, of course, is a disease of children. Occasionally we see osteoporosis in adults but as yet we do not know what relation this has to a lack of vitamins.

It was very interesting to me some time ago to see in one or two journals, an offer by one of the companies that make vitamin concentrates, to give $10,000 to any man who will show that Vitamin D is of any value in the case of adults. I think such an offer supplies eloquent proof of the fact that we are still in ignorance on this point.

I rejoice that we have been given some answer here today to that important question: Do the man and his wife and his children who eat enough of many foods and who are well nourished, have to be worrying about the addition of concentrated vitamins to their diet? I think Dr. Jeans is right when he says that except perhaps for seeing that the children have some Vitamin D, especially in winter, we do not have to worry.

Some people are certainly overdoing this vitamin business. I saw a woman the other day here in the Clinic who was taking, if I remember correctly, a quart of orange juice a day. Her dentist assured her that in this way she could cure her pyorrhea. She had been on this diet for several months but all it did was to produce a number of queer symptoms and some indigestion.

Unfortunately for those of us who would like to see our hospitalized patients or the patients recovering from a serious operation on the stomach get an easily digestible diet, the dietitians are usually so fearful that their patients will succumb to avitaminosis that the trays are covered each day with spinach and salads and fruit. Most of the dietitians I have met have acted each day as if the devils of avitaminosis were right on their heels, or as if their patients were but one jump ahead of an ambulance or a hearse. Actually, we know they are not in so precarious a state. In the old days, when a sailing ship took months to go around the Horn, the sailors who lived on salt pork and flour went weeks and months before they began to develop signs of scurvy.

There is another important thing we must remember in our practice of dietetics, and this is that in order to supply vitamins we do not have to fill the patient with indigestible roughage. I feel strongly that in prescribing diets we should think more about digestibility and less about the danger of the patient's dying with avitaminosis. If we want to give vitamins alone, we can give them in a concentrated form.

My time is almost up and there is just one more thought I would like to leave with you. What are vitamins? For the most part they are stimulators of growth in the infant and child. Well then, are not we

physicians and all pediatricians and all intelligent, college-bred mothers acting as if the most important thing on earth was to make the children grow as much as possible? And are we not doing this aimlessly and thoughtlessly and sometimes to the injury of the child? It may be all right to stuff children of small, short-statured parents with growth hormones, but is there any sense in doing this to the children of parents who are taller and heavier than the average? Do we want to make a boy so tall that he cannot fit into any bed or any theater seat or any Pullman berth? Do we want to make a girl so huge or so tall that her chances of marrying are greatly diminished?

As you all know, every generation in America is getting taller. My father is about five feet five inches and my mother was five feet six inches tall. I have a brother who is six feet one inch like me; another brother was five feet ten inches; one sister is perhaps five feet nine and one-half, and another is about five feet nine inches tall. Now, one of my boys is six feet two inches tall and one of my daughters is so tall that she had difficulty in getting dancing partners to suit her. She felt sometimes like suing me for damages for feeding her so well when she was a child. Now she has a husband six feet five inches tall and God knows how tall their children will be!

Similarly, I know two young people who are both much larger and heavier than the average run of humanity. Every day they cram their little girl with all the vitamins and cod liver oil and food that they can induce her to take. Even without such efforts the child might easily grow into an unpleasantly large woman, so why should that otherwise very intelligent mother be struggling daily to produce a baby whale? Obviously this phase of the subject has never occurred to her. Actually, the time may soon come when large people will go to physicians to find out how they can keep their girls from growing too tall and too big.

OBSERVATIONS ON THE DEEP Q WAVE IN LEAD III OF THE ELECTROCARDIOGRAM*

JOSEPH F. BORG, M.D.†
Saint Paul

RECENT electrocardiographic literature has called attention to the probable significance of a deep Q_3 wave in the diagnosis of myocardial disease. Investigators of the electrocardiogram in coronary occlusion have demonstrated the comparative frequency of this finding in their records without calling notable attention to it. Thus Parkinson and Bedford[7] noted a deep Q_3 in nine of twenty-eight cases of coronary occlusion, and, in six of twelve recorded electrocardiograms demonstrating coronary occlusion changes, as recorded by Barnes and Whitten,[1] this is to be found.

However, Pardee[6] first set forth the criteria by which significant Q_3 waves were defined, and these have been accepted by those who have discussed the subject. These criteria follow: (1) the initial deflection of QRS must be downward and there must be no S wave; (2) this wave must show 25 per cent or more of the greatest excursion to be found in the QRS of any lead; (3) records must be of normal or left axis deviation; and (4) records with a notched QRS, the so-called M or W complexes, must be excluded (Fig. 1).

The rarity of a deep Q_3 wave in normals is indicated by the finding of only two in 1,103 normals by Edeiken and Wolferth,[2] both of whom had horizontally placed hearts, a condition known occasionally to produce a deep wave when marked. However, Ziskin[9] found 20 electrocardiograms of 86 with deep Q_3 waves to be in normals, which he attributed to a horizontal heart position.

The present study covers 1,819 electrocardiograms from private and public practice, 78 patients showing deep Q_3 waves (Table I), distributed as follows: 1.33 per cent of 1,204 patients in private practice, 11.1 per cent of 63 patients in private hospital practice and 9.6 per cent of 552 patients in public hospital practice. There were forty-five men and thirty-three women, varying in ages from nine to eighty-one, 73 per cent of whom were over 50 years (see Table II). This represents an incidence of 4.3 per cent in a fair cross-section of all types of practice where electrocardiography was used, comparing with 4.1 per cent of Edeiken and Wolferth,[2] 7 per cent of Pardee,[6] and .04 per cent of Willius.[8] The latter's significance is probably due to the factors influencing the 1.33 per cent in private practice in this series, namely, the taking of electrocardiograms wherever a possible heart disease was suggested, and thus naturally including a large number of normals or cardiac neuroses.

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†Assistant in Medicine, Medical School, University of Minnesota.

Of the seventy-eight records only one was found in a normal individual, that in a boy of eleven years. The anginal syndrome was found in forty-one patients, of whom seven had coronary thrombosis. Hypertensive heart disease or coronary sclerosis, or both combined, was found in forty-two patients. Some of the angina pectoris patients are also included under the latter diagnoses, but in all 75.1 per cent were with definite diagnosis of degenerative cardiovascular disease. The remainder were divided as shown, the only significant group being the rheumatic heart disease with seven patients.

That many of these patients had an advanced grade of heart disease is shown by the fact that 43.6 per cent were decompensated when examined. Also of prognostic value may be the fact that twenty-three, or 29.4 per cent, died within three years, all dying of their heart disease. All of the rest of the deaths were also due to cardiac decompensation. Attention may be called to two patients with angina pectoris and coronary occlusion, both over fifty years of age, one of whom died after nine years of angina pectoris and the other of whom is living and working today. Nevertheless, these observations show that this finding is frequently found in patients with heart disease of poor prognosis.

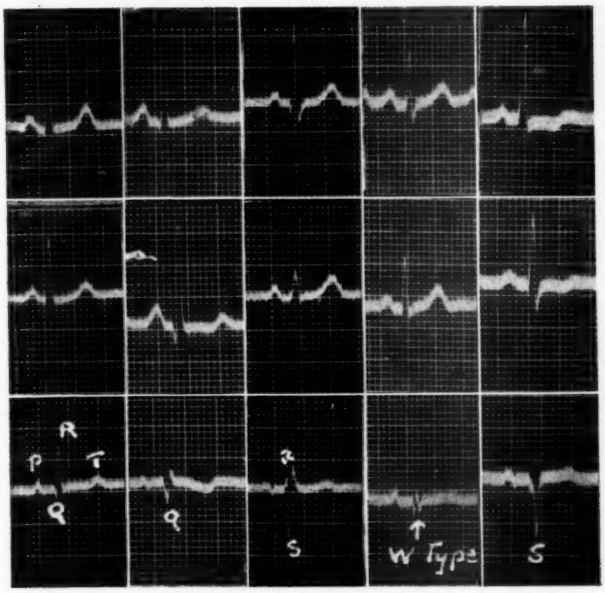

Fig. 1. *A.* A normal electrocardiogram. Very small Q wave is present in Lead I.

B. A well marked Q wave in Lead III but less than 25 per cent of the greatest QRS excursion.

C. A deep S wave in Lead III with a very short preceding R wave; not to be confused with a deep Q_3.

D. The W type of QRS complex in Lead III. This and the M shaped complexes are excluded from consideration.

E. A true deep Q in Lead III. There is no preceding upward deflection of QRS and the Q wave is practically 50 per cent of the greatest deflection of QRS in any lead.

Of especial interest is the fact that twenty-three, or 30 per cent of all the patients with heart disease, showed otherwise normal electrocardiogram, including three patients who died, one suddenly from angina pectoris, one from decompensation in hypertensive heart disease and one from arteriosclerotic heart disease with decompensation. Other authors show 45.6 per cent (Edeiken and Wolferth[2]) and 66 per cent (Willius[8]) of these patients investigated to have no other associated electrocardiographic abnormality, probably influenced by the type of patient, it being true the great majority of this series of patients had an advanced type of disease, with a

TABLE I. SUMMARY OF CASES

		Total	Private	Ward and Clinic
	Number of Cases with Deep Q_3	78	24	54
Anginal Syndrome	Angina pectoris	34	10	24
	Coronary occlusion	7	3	4
	Hypertension and (or) arteriosclerosis	42	9	33
	Rheumatic heart disease	7	0	7
	Syphilitic heart disease	1	0	1
	Hyperthyroidism	1	0	1
	Myxedema	1	0	1
	Chronic myocardial disease cause unknown	4	0	4
	Decompensated when seen	38	8	30
	Died	17	4	13
	No heart disease	1	1	0

TABLE II. AGE DISTRIBUTION

Age	Number	Per cent
10–20	3	3.9
20–30	3	3.9
30–40	4	5.2
40–50	11	14.3
50–60	20	26.
60–70	23	29.9
70–80	13	16.9

TABLE III. T WAVE NEGATIVITY—A COMPARISON

T Wave Negativity	Pardee No.	Pardee %	Willius No.	Willius %	Borg No.	Borg %
Lead I	1	2.5	28	9.3	3	3.8
Leads I and II	4	9.0	20	6.6	20	25.6
Lead II	0	0	0	0	3	3.8
Leads II and III	11	25.0	27	9.0	5	6.4
Leads I, II and III	0	0	11	3.7	7	9.0
Total	16	37.2	86	28.6	38	48.7

TABLE IV

	Total with significant Q_3 waves	Anginal Syndrome No.	Anginal Syndrome %	Hypertension and (or) arterio sclerosis without the anginal syndrome No.	Hypertension and (or) arterio sclerosis without the anginal syndrome %	Syphilitic cardio-vascular disease No.	Syphilitic cardio-vascular disease %	Rheumatic heart disease No.	Rheumatic heart disease %
Pardee; No. of cases not stated	43	27	63.0	2	4.6	1	2.32	4	9.3
Edeiken and Wolferth; 500 cardio-vascular cases	31	5	16.0	10	33.0	8	25.8	3	9.7
Willius; 70,000 electro-cardiograms	300	115	38.3	153	51.0	7	2.3	8	2.7
Borg; 1819 electro-cardiograms	78	41	52.3	42	53.8	1	1.3	7	8.9
Ziskin; 4,885 electro-cardiograms	86	12	14.0	41	48.1	0		3	3.5

higher probability of other findings. This would lead one to be suspicious of heart disease in records showing the deep Q_3 wave without other electrocardiographic abnormality. In about half of this series (48.7 per cent) there was significant T wave abnormality associated. This is given in Table III with a comparison of the findings in the series of Willius[8] and Pardee.[6] Considerable variation is seen here but probably the larger number of these findings is again due to the advanced grade of heart disease predominating in this series. Other abnormalities noted were eight electrocardiograms with delayed auriculo-ventricular conduction, seven with arborization defects of QRS, six showing an abnormally low voltage, eleven showing auricular fibrillation, 6 showing ventricular extrasystoles and seven showing the arched S-T interval characteristic of coronary occlusion. Three of the patients with this last finding have died.

A study of the relationship of the depth of the Q_3 waves to the clinical diagnosis revealed nothing significant except for a tendency for the deeper waves, the 75 to 150 per cent type, to be associated with coronary occlusion and sclerosis.

DISCUSSION

Bringing together the results of the previously reported and present series, as regards the more important conditions, it can be seen that there is a general agreement in the fact that this wave occurs chiefly in patients with degenerative cardiovascular disease (Table IV). Undoubtedly variations in the type of material used plays a

part in the varying results here found, as in the relatively high percentage of syphilitic heart disease found by Edeiken and Wolferth[2] alone. This type of disease was relatively infrequent among the patients studied in the present series. This table also shows the high percentage of anginal syndrome generally associated with this wave, although the actual figures varied. Ziskin admits a general younger age in his group than that usually associated with anginal syndromes. Possibly Edeiken and Wolferth's low figure[2] has a similar explanation on an age, sex or race basis, such information not being given. It may easily be that the criteria of the anginal syndrome (outside of coronary occlusion) may vary with different authors, and thus the consideration of all the degenerative heart disease in a single group may give a more accurate classification.

Considerable discussion of the probable mechanism of production of the deep Q_3 wave points to two probabilities: (1) involvement of the septum by cardiac disease; and (2) a change in position of the septum toward the horizontal. Lewis[4] attributes the Q wave to the septal activation, and the work of Pardee,[6] Meek and Wilson.[5] Edeiken and Wolferth[2] and Ziskin[9] point unmistakably to the rôle which a horizontally placed septum plays in the production of a deep Q_3. However, the striking results of Fenichel and Kugell[3] in the demonstration of septal myocardial damage post-mortem in patients showing the deep Q_3 cannot be ignored. It is definitely shown that the great majority of these patients have a serious myocardial disease. This is emphasized by the present series with its three year mortality of 29.4 per cent. Only further detailed necropsy study of these cases will further clarify the situation.

SUMMARY

1. Study of 1,819 electrocardiograms showed 78 presenting a significant deep Q_3 wave, occurring chiefly after 50 years of age and especially in public and private hospital practice.

2. The majority of these occurred in patients with degenerative heart disease.

3. The anginal syndrome was present in 52.3 per cent of the patients.

4. Histories of decompensation were present in 43.6 per cent of the patients.

5. Thirty-one per cent of the patients presented no other electrocardiographic abnormalities but all had otherwise proven heart disease, showing the difficulty of excluding such condition where the deep Q_3 may be found alone.

6. Death within three years occurred in 29.6 per cent of the patients whose electrocardiogram showed this finding.

7. The finding of the described deep Q_3 waves seems destined to be of considerable aid in the diagnosis of myocardial disease.

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918 LOWRY MEDICAL ARTS BUILDING

CALCIUM DEFICIENCY ASSOCIATED WITH FUNCTIONAL GASTRO-INTESTINAL DISTURBANCES IN ADULTS*

E. L. GARDNER, M.D.
Minneapolis

THE purpose of this paper is to call attention to the clinical manifestations of a group of adult patients with so-called "functional dyspepsias," who show definite evidence of bone decalcification by controlled radiographic studies. In order to evaluate the importance of the symptoms, the present knowledge concerning calcium metabolism should be briefly reviewed. Much confusion has arisen because physiologists, until recently, did not recognize that the minimum chemical requirements for maintaining life and growth were not the optimum requirements for the best health and maximum efficiency. The adult may maintain calcium equilibrium on 0.4 to 0.5 gram of calcium oxide per day, but for proper reserve power and resistance requires three times that much. The average American diet, according to Lusk, Sherman and others, often does not reach this minimum requirement, unless one pint or more of milk is added to the diet, or an equivalent of cheese. One litre of milk furnishes 1.4 grams of calcium and 1 kilo of cheese 5 to 10 grams. Other foods in the dietary contain much smaller amounts of calcium. In green vegetables there is an excess of magnesium over calcium, or the deficiency of phosphorus in a vegetarian diet makes calcium less available for use by the living organism.

Calcium is necessary to the body in the following chemical states:

1. Calcium carbonate and calcium phosphate of bones.
2. As a precipitate in tissue and organs in pathological conditions.
3. As a content of all tissue influencing the excitability of the motor system.
4. Indispensible for the normal clotting of blood.
5. Saponification of fats in the intestine.

Absorption and excretion of calcium: From 65 to 75 per cent of the calcium ingested passes out in the feces while 25 to 35 per cent is excreted in the urine. Only magnesium, in the body, has the same properties as calcium. Sodium and potassium, for example, are almost entirely excreted through the kidneys. Absorption of calcium is impeded by:

1. Diarrhea.
2. Insolubility of the calcium salt ingested.
3. Decreased inorganic acid content of the stomach and small intestine, as in deficient hydrochloric acid.
4. Too large an amount of phosphate in the food as it produces insoluble calcium phosphate.
5. Poor utilization of fats and fatty acids, because fatty acids in the intestine form insoluble calcium salts.

On the other hand calcium absorption is increased by:

1. Acidosis.
2. Acid (mineral) in the intestine (normal HCl).
3. Ammonium chlorine producing systemic acidosis.
4. Probably Vitamine 'D' and violet ray (Sunlight).

According to Zucker, on a well-balanced diet containing 1.5 grams of calcium daily, the human body excreted 71 per cent in the feces, and 29 per cent in the urine, but after ingestion of 300 c.c. of 0.1 n HCl the ratio was 68 to 32. Upon giving 15 grams of Na HCO_3 the ratio was 78 to 22 per cent. The urine normally maintains the balance.

According to experimental evidence most of calcium absorption probably takes place in the small intestine. Most of the calcium absorbed is excreted by the kidneys. According to the work of Wellman on rabbits, one-fourth to one-third of endogenous calcium was excreted by the intestine, while Dadlez recovered two-thirds of intravenously injected $CaCl_2$ in the feces and one-third in the urine.

In starvation, the calcium first disappears from the urine, but even after prolonged starvation, the feces show very considerable amounts thereby producing bone decalcification.

Distribution of blood calcium: Normal blood serum contains 9 to 11.5 mg. of calcium per 100 c.c. of blood, but blood cells are almost devoid of calcium. Only in extreme metabolic disturb-

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ances does the blood serum calcium vary from normal. In the terminal months of pregnancy there is a tendency to be slightly below the average normal. Edema fluid, serous exudates and spinal fluid contain 5 to 7 mg. per 100 c.c., the amount being higher with increased protein content.

Much clinical observation has been handicapped by the impression that probably no calcium disturbances could be present as long as the total serum calcium values were undisturbed. Fortunately for the animal organism it is only in extreme difficulties that the total serum blood calcium is disturbed, although bone may be decalcified and body tissues depleted.

No doubt, calcium exists in the blood in more than one physio-chemical state, and although the question of how many forms is uncertain, the bulk of evidence (see Peters and Van Slyke) suggests the following probabilities:

1. About 20 per cent appears in solution, the same as any other soluble salts, *i.e.*, in an ionized state.

2. About 25 per cent is held in solution by the serum proteins (colloidal).

3. And about 50 per cent possibly exists in a state similar to supersaturated solutions, and is probably under the influence of the parathyroid hormone.

Relation between calcium and phosphorus: Bivalent calcium and trivalent PO_4 in the circulatory serum seem to bear a reciprocal relation to each other. With decreased calcium the phosphates increase and vice versa. Decreased serum protein is also accompanied by decreased serum calcium, such as occurs in edema. Quoting Peters and Van Slyke, "Serum calcium values cannot be interpreted unless both protein and phosphate are simultaneously determined or are known to be normal. Low calcium with low protein or high phosphate has an entirely different significance from a low calcium with normal protein and phosphate."

Does calcium deficiency occur and if so can it be recognized in ordinary clinical practice? To study a calcium-phosphorus balance, the patient must be hospitalized and accurate food, blood, urine and fecal analysis made, which requires the services of a well-trained bio-chemist. In actual practice, other methods of diagnosis must be employed as a rule. The following case of undoubted calcium deficiency will first be reported in order to keep the picture of the more extreme case in mind.

Case 1.—Mrs. I. first consulted us on May 27, 1927 when forty years of age. At this time she complained of: (1) stiffness of the body from the shoulders to just below the hips; (2) pain and soreness upon pressure over any part of the body skeleton; (3) recurrent diarrhea; (4) abrominal discomfort.

The patient was a graduate nurse who had been working off and on since her marriage six years before. The family history had no bearing on the complaint. As a baby the patient had suffered from rickets. She had a chronic appendix removed in 1910 and tonsillectomy in 1914. She had some tendency to urticaria. She had had two previous attacks of slight upper abdominal pain with cause undetermined.

The patient had had a tendency to diarrhea all her life, but in 1914 it was associated with soreness in shoulders, arms and hands which cleared up after tonsillectomy. In 1917 she had slight general soreness and shortness of breath which improved after removal of some bad teeth. Her health was then good up to the spring of 1921 just before her marriage. She first had severe diarrhea with six or eight stools per day which were very foul, sour and contained quantities of gas. Similar recurrences appeared about twice a year ever since. She was in bed six weeks in 1921, married in 1922 and then was free from symptoms for a few months, but had recurrences every spring. In 1924 during pregnancy she had no diarrhea, but had considerable digestive disturbances, and during this pregnancy the stiffness about the back and joints reappeared. She miscarried at eight months and was then better for a few months. In the spring of 1925 she had a violent attack of diarrhea which lasted six weeks. There was no fever and neither blood nor pus was noted in the stools. In February 1926, one year before she first consulted us, she had a mild attack of La Grippe which was followed by diarrhea and muscle soreness during March, April and May, and was followed by stiffness and soreness throughout the body lasting into the Fall.

The recurrent attacks of diarrhea and the "rheumatism" persisted up to the time she consulted us, but she had never had redness nor swelling of the joints, nor a fever of more than one-half a degree.

She had had no treatment, but had herself chosen a heavy vegetable and starch diet. She had had abdominal distension, more frequent stools with flatus in the latter part of the day; no vomiting, but an intensive desire for sour foods or drink. She stated she had a tendency to anemia, and in one attack the blood dropped as low as 25 per cent. Her weight had dropped from an average of slightly above 100 pounds (height 5 feet 3 inches) to 85 pounds.

Examination: The patient, upon first examination in 1927, was pale, sallow and emaciated. There was no large glands. The tongue was normal and showed no evidence of present or former glossitis. The gums were spongy and bled easily. She had had eight teeth

removed which were reported "soft." The thyroid was not enlarged, but a loud, blowing systolic murmur was present over the precordium, which was fairly well transmitted to the axilla; no signs of failing compensation. The lungs were normal. Tenderness and a sense of resistance was present over the course of the descending colon which could be rolled under the fingers. There was no pitting edema.

Upon examining the skeleton, no evidence of arthritis could be made out, but the lumbar and thigh muscles were so rigid that movements of both the lower spine and lower extremities were greatly limited. The patient's gait resembled that of a boy walking upon stilts. A careful examination of the nervous system was entirely normal, except for this spasticity and muscle-nerve irritability. Nothing abnormal was found in the pelvis.

Fig. 1. As compared with control, *C*, changes were slight but definite. After six months there was no difference between the patient and the control.

The stools, in 1927, were constantly strongly acid, showed enormous quantities of free fat, fatty acid crystals, starch and meat fibres. The urine showed no abnormalities in the routine examination. The hemoglobin varied from 50 to 70 per cent, the leucocytes from 4,000 to 5,000 but there always existed a tendency to a leucopenia at the expense of the polymorphonuclear cells which varied from 35.5 to 45.5 per cent of the cells counted. The erythrocytes ranged from 4,070,000 to 4,900,000. Hypochromasia, poikilocytosis, anisocytosis, and constantly a few macrocytes were observed. The polymorphonuclear cells showed a distinct shift to the right. The Wassermann and Kahn blood tests had been repeatedly negative. No free hydrochloric acid by the fractional method (no histamine injection) was found in the stomach content. The blood calcium was 8.8 as compared with the average of the controls of 10 plus. No phosphorus determinations were made. The alkaline reserve (Van Slyke) was 50.0 vol. per cent. There was no edema.

A careful radiographic examination of the gastrointestinal tract showed only hyperactivity of the whole digestive tube. The gallbladder could not be visualized after the dye.

The bony skeleton showed a most marked rarifaction especially of the spine and pelvis, but this could also be noticed in the extremities. No evidence of arthritis existed, but only a process of decalcification.

A proctoscopic examination showed a mild proctitis.

At the time we felt that the case was one of mineral deficiency, probably due to a great loss of and a lack of absorption of minerals, but our conclusions were reserved until after observation of the effect of prolonged treatment. The patient was put on a non-irritating died consisting of milk, lean meats, finely divided non-irritating vegetables, gelatine and a small amount of butter. Sugar was allowed, but starches were restricted to the minimum. Calcium salts (carbonate and phosphate) were given by mouth and parathormone for a few days. Hydrochloric acid was administered with meals. To this treatment was added either sun light or quartz lamp. Six weeks of treatment raised the blood calcium to 10.1 mg. and repeated examinations since show values running from 10.0 to 10.4 mg.

Improvement was gradual but most gratifying, and, after six months, the patient has constantly served as a health nurse in a large department store. She is able to prevent recurrence of symptoms, but upon one occasion after being careless about her routine, she had a recurrence of the diarrhea and general body soreness. The blood calcium is now normal and the stools are free from fat. The x-ray films still show poor calcium of the bones of the hand as compared with the average normal control.

Discussion.—This patient's history and findings conform very well with the condition frequently described as "non-tropical sprue." A most carefully studied case is reported by Marble and Bauer in 1931. These authors carefully reviewed the literature and reported a case in which for the first time careful calcium and phosphorus metabolic studies were made. The patient was a man of thirty-nine who had had diarrhea for three years. Previous to that time he had had many mushy stools daily. The only known cause seemed dietary, but when the patient reported for examination the picture was that of (1) emaciation, (2) profuse diarrhea, (3) weakness, (4) marked caries of the teeth, (5) decalsification of the bones, (6) tetany, (7) achylia and (8) acid, fermentative stools, containing yeast-like organisms and an excess of neutral fat and fatty acid crystals. The patient's blood serum calcium was 6.7 mg. and serum phosphorus 1.28 mg. per 100 c.c. of blood. Their patient showed a mild pitting edema with lowered serum protein which probably accounted for a small part of the lowered blood serum cal-

cium. Their patient showed poor intestinal absorption of calcium and phosphorus even on a high diet. Almost all of these elements were excreted in the feces.

After their study they concluded that the conditions which hinder the absorption of calcium and phosphorus from the gastrointestinal tract eventually result in calcium deficiency and tetany, a type which can be differentiated from that of parathyroid insufficiency.

	Non-tropical sprue	Hypoparathyroidism
Serum calcium	Low	Low
Serum phosphorus	Low	High
Calcium excretion in feces	Increased	Normal
Phosphorus excretion in feces	Increased	Normal
Urinary calcium and phosphorus	Decreased	Decreased
Bone density	Decreased	Normal

After Marble and Bauer

The conditions which they believe led to the tetany of sprue are:

1. Dietary insufficiency of either calcium or phopsorus.
2. Deficiency in Vitamin D.
3. Diets containing a great excess of calcium over phosphorus and vice versa.
4. Long standing diarrhea.
5. Any disease hindering absorption from the gastrointestinal tract.
6. Long standing biliary or intestinal fistulas.
7. Excessive excretion of fat.

The blood in the typical cases may or may not be megaloblastic, but most of the recent cases treated are reported improved after feeding liver or liver extract.

Let us now contrast with non-tropical sprue the following cases which typify a large group.

Case 2.—Mrs. M. E. G. was first seen in 1925 when fifty-one years of age complaining of: (1) recurrent lower abdominal pain; (2) palpitation and rapidity of heart action; (3) muscle tremor.

She had never been seriously ill before and until the present trouble had had no confining illness. Her family history had no bearing on the present complaint. Her husband was dead and she had to support three children. Menstruation had stopped two years previously and she had been nervous ever since.

About six years before she consulted us she had some chronic intestinal indigestion with flatulence, epigastric pressure, soft stools and fatigue. She had always eaten large quantities of bread and potatoes. One year after the onset of the digestive symptoms, she began to have aching pains along the arms and legs, and fearing arthritis began to use cathartics, although never constipated before. For two years she used castor oil every other day. Three years before we saw her she began to have insomnia, palpitation of the heart, and spells of tachycardia lasting from a few hours to several days. No irregularity had ever been noticed. About this time she began to use large quantities of bran and other coarse foods because she believed she was constipated and had been warned about constipation by her medical advisors. She never allowed herself to go beyond a day without a bowel movement, and was happier if she had two or three bowel movements per day. About six months after the heart symptoms first appeared she began to have tremors with the attacks; she shivered, but had no chilliness nor fever. This was usually followed by two or three soft stools and the spell would gradually disappear.

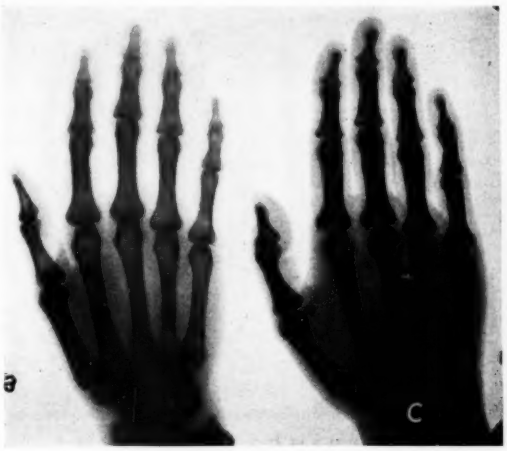

Fig. 2. Note decalcification as compared with the control, *C*.

She had had considerable abdominal soreness increased by laxatives, although laxatives relieved the general symptoms. Considerable gas was passed from the rectum and with the stools. At times she felt so sleepy that she was forced to lie down, a condition which was also related to the bowel function. She had been confined to her bed for weeks at a time because of heart symptoms and had been told she probably had serious heart trouble.

The physical examination showed a flabby, well nourished woman apparently moderately neurotic. The expression of the face was mask-like, not unlike that of early Parkinson's disease. The thyroid was slightly enlarged but no nodules were palpable. The gums were spongy, but the teeth, nasal sinuses and throat were

normal. (The tonsils had been removed one year before because of the pains). The blood pressure was 160/84 and there was a soft systolic blowing murmur at the apex of the heart, best heard in the axilla out-

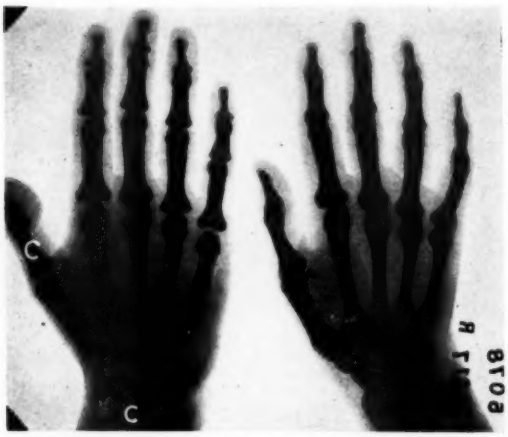

Fig. 3. A case similar to Case 2, which is reported.

side of the apex. There was no enlargement. The lungs were normal. The abdomen showed slight tenderness over the course of the colon. The pelvis showed nothing of importance.

The nervous examination showed exaggerated reflexes and muscle twitching, but otherwise entirely normal. Tenderness was present over the long bones and sternum upon pressure.

The blood showed moderate secondary anemia (hgb. 73 per cent; R.B.C. 4,500,000). The smear was normal, and the Wassermann blood test was repeatedly negative. The stools were strongly acid in reaction, fermentative and contained large quantities of undigested starch. The free acidity of the stomach contents was normal. The blood serum calcium was 10 mg. per 100 c.c. of blood.

The roentgen examination of the gastrointestinal tract was normal except for intestinal hyperperistalsis and hypermotility with spasticity at various locations.

This patient was unmistakably ill, although at the time we could only speculate as to the condition present. Organic heart disease was apparently excluded by observation and electrocardiogram. The patient was hospitalized and after prolonged observation we suspected there was some metabolic disturbance probably affecting the mineral balance, because the heart irritability, muscle tremors, and pain over the bones was very suggestive of a calcium and phosphorus disturbance.

The patient was placed on irritable bowel management, given calcium salts and sunlight. The symptoms completely disappeared after three months and the patient ever since has held a position as clerk of court. The bowels are regular and there are no cardio-circulatory symptoms.

Discussion.—This case is reported because it is the first patient (1925) in whom we suspected mineral deficiency in an apparently functional disturbance. She came from the northern part of the state where the water contains alkalies, especially magnesium salts. Cattle in the same locality, although given a well-balanced ration, have gradually developed a peculiar softening of the bones, especially in the second and third generations, which has been attributed by Dr. R. A. Gortner and associates as probably due to an excess of magnesium salts in the diet. Magnesium and strontium have been shown to partially relieve parathyroid tetany but to less degree than calcium, and, as in these cattle which had a tendency to diarrheal stools, may prevent the proper absorption of calcium in the intestine. These deficiencies do not appear acutely, but are the result of long periods of calcium-phosphorus poor diet or too rapid elimination. This patient living in the same locality was susceptible to the influences suffered by the cattle, probably had an increasingly negative calcium balance which was exaggerated by the high vegetable diet and excessive use of cathartics. Although vegetables contain considerable calcium, the magnesium is far in excess. The treatment was nothing more than a retracing of steps in the history. The results were suggestive.

Case 3.—Mrs. G. N. D. was first seen at her home September 21, 1931, when forty-one years of age, complaining of fatigue, palpitation of the heart, chronic indigestion, various pains in the extremities and mental depression.

The family history had no bearing on the case except that she had five children, and in spite of ideal hygienic care there had been rickets in two of them and one had had several fractures of the bones.

The present complaint began about four years previously, but symptoms were attributed to the fatigue of frequent pregnancies and social duties. The first symptom was fatigue and indigestion associated with belching and passing of gas. The appendix was removed and she was better for a year or more. One and one-half years previous to the present complaint she became very fatigued, had indefinite indigestion and was forced to bed for a rest. The heart became rapid and irregular. She then had short periods of improvement, but for the most part had been confined to her room. Because of the indigestion, she had daily for several months taken milk of magnesia, low caloric intake and a low mineral content diet. Menstruation had recently become frequent and copius. She complained of many "rheumatic" pains, and there was definite bone tenderness.

The physical examination showed signs of extreme fatigue, but mentally the patient seemed stable and unusually intelligent. She was well nourished but flabby, and there was a tendency to an excess of fat distribution about the pelvis and thighs. The gums were spongy and there was some retraction. She had had trouble with progressive caries. The thyroid was slightly enlarged, but contained no nodules. The heart was not enlarged, but a soft blowing systolic murmur could be heard over the apex. There was some tachycardia and an occasional extra systolic arrhythmia. The abdomen was negative except for tenderness over the course of the colon. The pelvis was normal except that the uterus was slightly enlarged and rather firm. Examination of the nervous system showed very active reflexes. The blood pressure was 118/76.

The blood, urine and blood calcium were normal. The stools were mushy, acid in reaction and showed the signs of marked starch fermentation.

The gastro-intestinal examination showed a poorly functioning gallbladder, but no shadows to suggest stones. The stomach outline was normal, but the small intestine showed very marked activity and the colon had eliminated a large part of the barium meal within twenty-four hours. The stomach contents showed a constant decrease of free hydrochloric acid. The x-ray of the hands with a normal control showed a definite decrease of calcium salts.

We suspected in this case a calcium deficiency related to excessive bowel activity and the long use of magnesium as a laxative.

Treatment consisted of giving calcium salts, liberal vegetable and milk diet, and the elimination of all cathartics. Recovery was complete at the end of six months and the hands showed a return to normal calcium density.

Discussion and Summary.—These last two cases are typical of a considerable group of cases which we have studied during the past five years. The symptoms seem to occur so frequently that they probably indicate a clinical entity. Unfortunately, no complete metabolic studies could be made, for obvious reasons. A typical hypothetical case might be described as follows:

Possibly in a family where there is a history of infantile rickets or spasmophilia, in spite of good living conditions, an adult patient begins to have symptoms of indefinite indigestion associated with signs of increased intestinal peristaltic activity with mushy or alternatingly mushy and spastic stools, or a recurrent diarrhea. Defecation is often explosive and accompanied by the passing of a large amount of gas. The stools are for the most part strongly acid in reaction with a sour, yeast-like odor. Large quantities of undigested starch associated with yeast-like organisms and more frequently clostridia are noted in most cases if the stools are repeatedly examined when fresh. An increase of fatty acids and sometimes neutral fat may be found in the more severe cases. The patients after some months usually complain of dull headaches, sleepiness, lassitude and body soreness. Tenderness is frequently present over the long bones and muscles. Spongy gums and rapid caries may appear for the first time or may have been present for years before. The patient may complain of frequent canker sores or in the more serious cases a definite glossitis may appear. Because of the symptoms and especially because of the periods of spastic stools with distress, the patient begins to take cathartics which whip up an already present intestinal hypermotility. This catharsis, especially if the drug contains magnesia, apparently increases the symptoms. There is increasing physical debility and nervous depression. Muscle twitching and sometimes tremors appear, usually associated with an irritable heart action. Fundamentally, these patients usually do not belong to the visceroptotic asthenic type, but more frequently to the intensive intelligent type and, when well, are remarkably free from complaints and symptoms of neurasthenia. In other words they more frequently belong to the intensive "go-getter" type of individual. Sometimes the symptoms seem to be increased by pregnancy, and very often are worse in the summer months when on a high vegetable diet. Many of the patients seem to have had an aversion to milk and cheese throughout life, and probably have always been on a relatively low calcium diet.

The stomach contents may show an achylia, decreased free hydrochloric acid or a normal acidity. The total blood calcium is normal but often near its lower value.

Any condition which whips up intestinal peristalsis or prevents absorption accentuates the symptoms.

Some of the women, especially those over forty years of age, have menorrhagia. The basal metabolism is frequently slightly below normal. The blood may be normal, show a slight secondary anemia, or occasionally show many macrocytes.

If, upon radiographic examination of the bones, especially the hands, there is a definitely decreased bone density as compared with carefully picked controls, the diagnosis seems very likely. The increased bone density and the dis-

appearance of the symptoms with the improvement of general health when upon treatment makes the diagnosis much more certain. This condition can only be suspected in the earlier stages before the withdrawal of calcium from the bones, but a therapeutic test is justified. Deductions, however, from such results can only be reserved.

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CASE REPORTS

COARCTATION OF THE AORTA*

REPORT OF TWO LIVING CASES

M. J. SHAPIRO, M.D.
Minneapolis

Recently I[3] discussed the subject of "Coarctation of the Aorta" and presented the case history of a boy now seventeen years of age who has been under my observation for more than ten years. Since presenting this case I have had the opportunity of studying another case of the same type in a boy six years of age. It seems of value to report the six year old boy. I believe he is the youngest living case to be reported.

As was pointed out in my previous article, Bonnet divided all cases of congenital stenosis of the aorta into two main groups, infantile and adult. The infantile type consists of a diffuse narrowing of the isthmus of the aorta. The adult type includes those cases which present a sharp constriction of the aorta even to the point of a complete atresia in the region of the insertion of the ductus arteriosus. It was the impression of the older writers that adult coarctation of the arota was due to a fibrosing process in the aorta which was carried over from the normal post-natal fibrosis which occurs in the ductus arteriosus. Evans[1] has recently presented a number of reasons which he believes is good presumptive evidence that adult coarctation is due to maldevelopment of one of the branchial arches rather than to any post-natal fibrosis.

Evans has divided the adult type into six groups, the first three of which are of practical importance. Type I consists of a stenosis of the aorta in the region of the ductus arteriosus, patency of the ductus arteriosus, and hypoplasia of the proximal aorta. In this type the development of collateral circulation is unnecessary as the blood is shunted through the patent ductus arteriosus into the pulmonary circulation resulting in hypertrophy of the pulmonary artery which is usually larger than the aorta and in a right sided hypertrophy of the heart with usually a hypoplasia of the left ventricle. Type I is difficult to diagnose clinically as none of the characteristic vascular signs of the other two types are present. However, the patency of the ductus arteriosus can be diagnosed and the stenosis of the aorta may be suspected from the more or less characteristic x-ray picture.

Type II and Type III differ only in degree of stenosis of the aorta. In Type II there is a marked stenosis, the ductus arteriosus is closed, the proximal portion of the aorta is hypertrophied. In Type III the same conditions prevail but there is a complete atresia of the aorta close to the insertion of the ductus arteriosus.

It is my impression that the two cases I am to present belong to Type III. I believe they have complete atresia of the aorta and that the ductus arteriosus is closed in each case.

The first boy, who is now almost eighteen years of age, has unusually high color to his face. He appears to be unusually well. There is a marked pulsation of the vessels of the neck and episternal notch. Examination of the heart reveals enlargement to the left. The heart sounds are regular and pounding. At the apex and over the aortic area a blowing systolic murmur is heard. At the back of the chest on either side of the vertebral column a prolonged hemic type of murmur is heard which is quite characteristic of this condition. In fact, it is this murmur in my second case which led me to suspect the correct diagnosis. Because of the obesity it is impossible to see the enlarged collateral vessels on this boy's chest, but on palpation a number

*From the Lymanhurst School Heart Clinic, Minneapolis, Minnesota. Read before the Minnesota Society of Internal Medicine, Minneapolis, May 15, 1933.

of thickened, enlarged, rather tortuous pulsating vessels can be made out, especially on the posterior chest wall. If one runs the hand down this boy's body it will be noted that a distinct and remarkable drop in temperature is noted at about the waist line and especially over the left buttock. This is especially well brought out with the patient in a cold room. While the radial pulse is full and bounding the femoral and popliteal pulsations can not be palpated. The blood pressure in the right arm is: systolic 204, diastolic 100; left arm, systolic 185, diastolic 100. The blood pressure in the legs can not be obtained. The electrocardiographic tracing is normal. The roentgen examination reveals a second degree "hypertension heart" with characteristic left ventricular enlargement and erosion of a number of the ribs; the erosion of course, due to the enlarged intercostal arteries. The normal aortic knob is not present (Fig. 1).

Fig. 1. Six-foot radiograph of the heart of an eighteen-year-old boy with coarctation of the aorta which reveals left ventricular hypertrophy and several areas of erosion in the ribs as indicated by the arrow marks.

Fig. 2. Six-foot radiograph of the heart of a six-year-old boy with coarctation of the aorta which reveals beginning left ventricular enlargement and also shows several areas of erosion in the ribs as indicated by the arrow marks.

Fig. 3. Visible and palpable enlarged collateral vessels in the posterior surface of the chest in a six-year-old boy with coarctation of the aorta.

The second boy is six years of age and he, too, appears to be unusually well. He was referred to the clinic because of a "murmur in his heart." Clinical examination of his heart reveals no marked enlargement, a systolic rather short murmur is heard over the apex and over the aortic area. At the back can be heard the characteristic hemic murmur on either side of the spine exactly the same as in the previous case. On careful inspection in favorable light a number of pulsating dilated vessels can be made out in the intercostal spaces posteriorly. I have chalked over these vessels to make them stand out more clearly (Fig. 2). As in the first case the radial pulse is full but the pulse in the lower extremities can not be palpated. The blood pressure in the arms is: systolic 134, diastolic 80. It can not be obtained in the legs. There are no surface temperature abnormalities in this case. The electrocardiogram is normal. The roentgen examination reveals slight enlargement of the heart, which shows a tendency toward a left ventricular enlargement. Careful inspection will reveal a number of areas of erosion in several ribs. It is rather remarkable that this erosion should have occurred at so early an age (Fig. 3).

The diagnosis of coarctation of the aorta is made in both of these boys on the following diagnostic findings:

1. The establishment of collateral circulation as evidenced by the visability and palpation of the dilated vessels on the chest and by the characteristic hemic murmur heard over these vessels and also by the erosion of the ribs as revealed in the x-ray film.
2. The increased blood pressure in the upper extremities and the absence of blood pressure in the lower extremities.
3. The left ventricular hypertrophy revealed by the x-ray film, and the absence of the normal aortic knob. In the older boy fluoroscopic examination reveals an increased pulsation of the aorta to the right of the sternum. In the left oblique position a rather abrupt diminution in size of the aortic arch is made out presumably at the point of constriction.

It is my impression that these cases belong to Type III as described by Evans because there is no evidence of patency of the ductus arteriosus. The marked development of collateral circulation at so early an age makes the diagnosis of complete atresia of the aorta quite probable.

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ANIRIDIA*

VIRGIL J. SCHWARTZ, M.D.
Minneapolis

Aniridia is a term used to denote congenital absence of the iris, but it is entirely possible that section of an eye with this anomaly might show the root of an iris to be present. Clinically, however, the iris loss seems to be complete. One of the good recent accounts of this disease is to be found in Seefelder's chapter in Schieck and Bruckner's *"Kurzes Handbuch Der Ophthalmolo-*

*Read before the Minnesota Academy of Ophthalmology and Otolaryngology, February 10, 1933.

gie." The following discussion is based on liberal reference to this chapter.

Although the most conspicuous feature of aniridia is absence of the iris, it is usually associated with other abnormal findings such as visual impairment (usually pronounced), photophobia, nystagmus, anomalies of the lens such as total cataract, anterior and posterior polar cataract, dislocation, diminution in size, and anomalies of the suspensory ligament (ectopia of the lens). There may also be hypoplasia or aplasia of the ciliary processes and of the fovea centralis. Atrophic choroidal spots, vitreous opacities and detached retina may be found.

Fig. 1. Eyes of patient D. L., showing absence of iris.

Fig. 2. Eyes with normal irides.

Aniridia is more definitely hereditary than any other anomaly of the eye, at least in man. Thus Risley found 114 cases of aniridia in four generations of one family. In lower animals aniridia is but rarely seen. The simultaneous appearance of other malformations of the iris in aniridia families is especially interesting. Thus in an aniridic family observed by Clausen there was found a case of bilateral inferior coloboma of the iris, and another of slit-like defects of the iris stroma with an apparently intact layer of pigment epithelium. In another aniridic family reported by Lindberg, one child presented marked defects of the stroma layer and smaller defects of the pigment layer, the iris being of normal surface extent. In addition there were marked amblyopia, some nystagmus, lens opacities, and absence of the fovea centralis. This was also the case in the patient's brothers and sisters, who had complete absence of the iris.

Microscopic inspection of eyes with aniridia has often disclosed the presence of a narrow stump of iris in more or less its entire circumference, even though clinically no iris could be seen. In some cases this root is attached to the posterior corneal surface as an anterior synechia, and in others the root projects free in the anterior chamber. In a number of cases the iris was, in fact, fairly broad; and yet, even in these there was no evidence of a spur of iris musculature, despite the fact there was ample room for it. However, von Bohm and von Hippel were able to demonstrate some evidence of atypically developed iris muscle. In a number of cases the angle of the anterior chamber was obstructed because of the unusual development of the uveal structures, or because of the adhesion of the iris root to the posterior surface of the cornea. Thus the comparative frequency of glaucoma in cases of aniridia may be explained.

A most important anatomic finding, which was also noted clinically by Velhagen and others, is the absence of the fovea centralis. This explains the loss of vision of aniridic eyes better than all the other changes, as, for instance, cataract. This visual loss is often present long before any appreciable loss due to the cataract may have set in.

Principally because of the absence of the fovea, and secondarily because of the changes in the lens and the zonule the theory is advanced that the entire group of defects found in aniridia may be traced back to a common origin, namely an arrest of development of the associated ectodermal structures (retina, lens, zonule). This arrest may not be equally marked in all areas. The most weighty objection to this view is that of von Bohm, who feels that aniridic eyes with good vision, as occasionally observed, do not fit in with Seefelder's theory, for as a matter of fact, in a number of cases such high visual acuity has been found (in one case it was 20/20) that an aplasia of the fovea is out of the question. However, as opposed to these patients with comparatively good vision there is a great preponderance of those with poor sight. In most cases the low degree of visual acuity cannot be explained by the lens opacities. At birth and in the early years of life these opacities seem to be of little consequence, so that the nystagmus must be due to some other cause. Further, young individuals who have a well developed fovea and who later develop opacities of the media (as for instance, zonular cataract), do not develop nystagmus even when the vision becomes markedly reduced. Lindberg's case showed that the iris might be comparatively well developed and the fovea absent. Seefelder does not believe that aniridia may be due to mechanical hindrance to development of the iris by excessively long contact of the lens with the cornea.

The history of the case reported herewith is as follows:

D. L., a boy of six, was admitted to the clinic June 21, 1932. He is one of three children, the other two being normal girls. This child is in good health except for his vision. He thinks that he sees better when he is close to objects than at a distance. He now has occasional headache. Bright light used to trouble him greatly as a young child, but not now. He has just recovered from scarlet fever.

A general physical examination was made August 2, 1932, and he was found to be entirely well. External examination of the eyes showed the following: (1) apparently total absence of the iris in both eyes; (2) an oval cataractous opacity in the central part of the right lens about 3 x 5 mm.; (3) optical nystagmus, and under cover each eye turned out about ten degrees; (4) form fields normal in both eyes; (5) visual acuity of 6/200 in each eye; (6) normal tension.

A diagnosis was made of aniridia, complete and bilateral, and of cataract of the right eye.

He had been wearing O.D. + 1.50 S. $\supset$ + 2.00 C. x 90 which gave him 10/200 vision, and O. S. + 2.00 S. $\supset$ + .75 C. x 90 which gave him 20/200. I have already stated that his uncorrected acuity was 6/200 in each eye. On June 28, 1932, a refraction was attempted without a mydriatic, as a matter of interest, but the ciliary muscle was so active that satisfactory retinoscopy could not be done. Under atropin a week later he accepted O. D. + 2.25 S. $\supset$ + 1.25 C. x 115 to get 20/100 vision, and O. S. + 2.00 S. to get 20/100 vision also. Further improvement was not possible.

FOREIGN BODIES IN THE BLADDER*

E. C. Robitshek, M.D., F.A.C.S.
Minneapolis

Foreign bodies,† other than vesical or renal calculi, include a large variety of articles, the same gaining access to the bladder by various methods. A bullet may lodge in the bladder or a portion of clothing or bone may be carried into the bladder by a bullet or by some other penetrating objects. Also a foreign body may ulcerate into the bladder from the intestine or from the peritoneum, or a foreign body may cause a puncture wound of the perineum or of the abdominal wall, enter the bladder, break off and a portion of it remain behind. Such foreign bodies may be sticks of wood, branches of shrubs or trees, or pointed metal objects, teeth or hair from a ruptured dermoid cyst. Again, foreign bodies may enter the bladder through a fistula. However, most foreign bodies enter the bladder through the urethra. Portions of old and rotten catheters and filiform bougies have thus, not infrequently, been found. The great majority, however, have been introduced by individuals either in curiosity, or from morbid sexual motives. The latter class of accidents are much more frequent among women than men. Such foreign bodies inserted into the urethra usually accidently slip out of reach and into the bladder. Among such bodies introduced for such purposes may be mentioned hairpins, pencils, sticks of sealing wax, chewing gum, beads, shots, catheters, bougies, straws, feathers, clinical thermometers, glass rods, wax tapers, stems of plants, sprigs of wheat, pieces of slippery elm, pork rinds, pieces of tar, needles, common pins, safety pins, penholders, pencil cases and toothbrush handles. Gross found three caudal vertebræ of a squirrel in the center of a vesical calculus taken from the bladder of a man age thirty-five. It was afterwards elicited that the patient had practised masturbation with the tail of this animal. Sharp and irregular bodies may cause pressure ulceration and even perforation with infiltration of urine. Needles may become embedded in the bladder wall.

A few months ago I was called hurriedly to examine a young man who was bleeding from the urethra. I found him to be a white man, aged nineteen, a kitchen helper and a waiter in a boarding house. His appearance was pale, and anxious, although he was not complaining of any severe or sharp pain when resting quietly. His present complaint consisted of a sudden bleeding from the urethra. He did not know how much blood he had lost. Blood appeared also when he urinated.

Examination revealed a normal temperature and pulse of 78. His past history was essentially negative. Examination revealed some oozing of blood from the urethral orifice and some dry blood on the head of the penis. My first impression was that the patient was suffering from a papilloma of the bladder. However, further examination of the external genitals disclosed a definite hard object to be felt in the perineum. This, the patient then told me, he had also noticed. A digital rectal examination confirmed this finding.

I now requested that the patient enter the hospital for x-ray examination. Further questioning disclosed no evidence of what had evidently taken place and the only answer that I could get to my several questions, was always the same, "that he had swallowed some glass ten years ago," and in this answer I presume he wished to give me a clue. The x-ray film as shown here reveals distinctly a broken off piece of glass tube or glass catheter, definitely within the bladder and the broken off portion pointing towards the urethra.

Under spinal anesthesia and assisted by Dr. Mackey, a suprapubic cystotomy was performed, the glass tube found, firmly lodged in the bladder and removed without any special difficulty. The bladder was closed in the

usual method without drainage, except for a small rubber tube placed for temporary drainage in the space of Retzius. He made an uneventful recovery and left the hospital in the usual post-operative period. Cross examination of this patient, following his operation, could not sway him from his former and persistent statement, "that he had swallowed some glass ten years previously."

*Read at the regular staff meeting at the Eitel Hospital, Minneapolis, May 19, 1933.

†Gould, G. M., and Pyle, W. L.: Anomolies and Curiosities of Medicine, p. 676, 1897.

KOREMLU

The *Chicago Tribune* of Sunday, July 17, 1932, issued the statement that a voluntary petition in bankruptcy was filed by Koremlu, Inc., depilatories, of 11 West 42d street, listing liabilities of $2,448,745 and assets at $2.93. There seems to be accumulating evidence, however, that the individuals, or at least some of the individuals, who have been connected with the exploitation of Koremlu as a depilatory have decided that there is too much money to be made in the depilatory business to abandon it, even if dozens of women have been injured by their old product. There is now appearing on the market an alleged depilatory called "Croxon" which emanates from the same office as that of Koremlu. Croxon, Inc., was brought into existence January 29, this year, and the president of the concern is said to be one A. W. Lublin. According to an advertisement, Croxon "will permanently destroy both hair and roots in three to six months. Even though we are not yet in a position to publish the complete composition of Croxon, it is our opinion that Croxon will not destroy both hair and roots, either in three months or three years. (Jour. A. M. A., July 30, 1932, p. 407.)

PRESIDENT'S LETTER

To the Physicians of Minnesota:

Within a few days the annual Christmas Seal sale will be taking place throughout the State. The sale of these seals is the sole support of the Minnesota Public Health Association and its constituent county tuberculosis associations.

There is no other public health education program in Minnesota and elsewhere that is so important and so deserving of the support of the physicians as this one.

Let us as an organization and as individuals do all that is possible to aid this program of education against tuberculosis and coöperate in every way in the Christmas Seal sale.

Yours very truly,

H. O. Pearce

President,
Minnesota State Medical Association.

EDITORIAL

MINNESOTA MEDICINE

Official Journal Minnesota State Medical Association, Southern Minnesota Medical Association, Northern Minnesota Medical Association, Minnesota Academy of Medicine, and Minneapolis Surgical Society.

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J. R. BRUCE, Business Manager
324 Fourth Avenue South, Minneapolis, Minn.
and
2642 University Avenue, Saint Paul, Minnesota
Telephones *Dupont 1013*
Nestor 1381

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Vol. XVI November, 1933 No. 11

SHALL I STUDY MEDICINE?

The choosing of a vocation is almost as important a step in the life of a young man as selecting a wife. The youngster is not likely to adhere to his early ambition to become a fireman or an aviator, and the grade school boy who knows what he wants to do or be when he becomes a man is an exception. Occasionally a boy's career is planned for him by a fond parent, but only occasionally does such a career materialize. Studies in high school and even in college usually are chosen only in a general way, with a definite career in mind. Often no greater tragedy can occur than the thwarting of a distinct inclination or ambition on the part of a boy to follow a definite career.

It is said that the practice of medicine used to be very much like the ministry as far as financial return was concerned. It may have been. Certainly in recent years, mercenary motives have influenced the youth of this country in their choice of medicine as a career. It is safe to say that the majority of such have been disappointed. On the other hand, it is probably true that a young man of average intelligence and industry could feel assured that the chances of making a fair living would be as good in the practice of medicine as in any other profession or commercial career.

The warning has been issued in various quarters that the medical profession is overstocked and that young men should be discouraged from entering the profession for their own good and the good of the profession. It is true that the country could get along with fewer physicians. The estimate has been made that there is about one physician for every 720 people in this country, a much higher ratio of physicians to population than in many civilized countries and about twice as many as in England and Wales. Last year there were daily over 15,000 patients in government supported hospitals in Minnesota, compared with some 20,000 in private hospitals. Probably it is a safe estimate that half of the population is not served by private practitioners. It would be interesting to know how many of the 157,000 licensed physicians in the country are in private practice and dependent on this half of the population for their livelihood.

There is danger that the present oversupply of physicians in the country may be aggravated by the situation in Germany. Jewish physicians have already left Germany, and doubtless a certain number will attempt to obtain licenses in the various states.

We must not be too pessimistic, however, in our advice to prospective medical students. What profession or industry is not crowded? A com-

parison* of the present status of the legal and medical professions, recently published, is of interest. The medical profession is in a far better situation than the legal profession as far as educational institutions and licensing are concerned.

Our medical schools number about half those existing in 1900, and 95 per cent of them are approved by our national association. The standard of medical education has been so raised in recent years and state license requirements are so exacting that few poorly prepared physicians are being admitted to practice. The number licensed last year is about the same as in 1904.

Less than half of the law schools, on the other hand, are approved by the national bar association. Admission to the bar is largely by examination with apparently little attention paid to where the applicant has received his preparation. Less than half of the examinations for admission to the bar in 1932 were passed.

While the number of physicians in the country has increased from 132,000 in 1900 to about 157,000 in 1933, the legal profession has increased in this period from approximately 107,000 to 175,000. Of course, once a man has prepared himself to practice medicine he is less likely to change his vocation, which is not true of the law graduate.

It is natural for a son to follow in his father's footsteps when it comes to the choice of a profession. This is very evident in the families of physicians. The idea of becoming a doctor has a distinct idealistic appeal to youth. Is there sufficient reason to discourage our sons from following in our footsteps? The less likelihood of large financial return in the practice of medicine in the near future will deter some whose only motive is financial. This will not be detrimental to the personnel of the profession, unless the encroachment of government and free medical care reaches the point where the opportunity of a fair return from the investment of money and time in a medical education will not attract the superior type of youth.

HIDDEN DANGERS IN VOLATILE GASES

There is evidence that the public has not received sufficient warning of the danger that exists to health and life in the careless handling of some of the new and old chemicals used in everyday life.

You purchase one of the newer fire extinguishers which is a liquid contained in glass bulbs. The bulbs are to be broken and the liquid scattered on the fire. You are told frankly that the bulbs contain carbon tetrachloride and you know you are paying an outrageous price, but the desire of protecting your home from fire leads you to be robbed knowingly. You are informed that the carbon tetrachloride will not stain or damage fabrics. But you are not informed that this liquid when exposed to flames is capable, like chloroform, of generating deadly phosgene fumes which in a closed space may be fatal. In a recent editorial in the *A. M. A. Journal* two fatalities are reported from the use of a patent preparation of carbon tetrachloride in extinguishing the burning clothing of two men.

Methanol can be bought in the bulk in the open market. How much warning is given the purchaser, we don't know, although when mixed with varnish the fumes are decidedly dangerous.

Many a housewife has learned from experience that the use of benzine and other cleaning fluids is very likely to produce a harmful effect if used in a closed room.

The widest publicity should be given to the danger that lies in certain of these liquids in common use. To be forewarned is to be forearmed.

DULUTH MALIGNED

The hay fever sufferers are leaving Duluth and the Arrowhead country. Very favorable reports are accumulating this year indicating that the efforts of the health commissioners of Duluth and a committee of the Chamber of Commerce have accomplished much in the cleanup campaign for abolishing baneful weeds and pollens. Duluth and the North Shore in some recent years suffered something of an abridgement of their former popularity with those condemned to seasonal allergic distress, whether it be ordinary hay fever, asthma or allied disorders. As agriculture developed south of Duluth and people became more careless of their own waste lands, the roadsides or gardens, the iniquitous ragweed and its associates made this less of a haven of relief for natives and visitors.

From all reports, however, a very great improvement has obtained, and whereas Duluth has

*Admission to the Professions of Medicine and Law: A Comparison Federal Bulletin, October, 1933. Reprinted from Notes on Legal Education, July, 1933.

never deigned to malign any other climatic zone (despite the lugubrious and studied weather insults hurled toward it; for example, the vaudevillian who amid the conceit of Kansas City said he had just come from a place up in the Far North, known as Duluth, "Where there is nothing between you and the North Pole but a screen door"), we announce a most successful hay fever season. Addressing that great crowd of perennial vacation seekers with the best excuse in the world—puffy turbinates and horrific nights—come to the North Shore next year and be happy! "The great open spaces" mean nothing—unless the upper air passages are included.

E. L. T.

CORRECTION

Attention has been called by Dr. O. McDaniel, Director of the Division of Preventable Diseases of the Minnesota State Board of Health, to an error as to the number of cases of syphilis on record with the Division cited in an article by Dr. S. E. Sweitzer entitled "Adequate Therapy of Syphilis," which appeared in the September number of MINNESOTA MEDICINE. The author stated that the cases seen at the Minneapolis General Hospital Clinic during 1932 constituted one-third of all the cases in the state in 1932. Instead, this number constituted a third of the cases in Minneapolis. The source of the error as to the figures has not been traced, but the correction should be, and is herewith, made.

Except in Minneapolis and Duluth venereal cases are reported directly to the Division of Preventable Diseases and the cases of syphilis reported in 1932 were: Minneapolis, 1,204; Duluth, 478; state (exclusive of Minneapolis and Duluth) 2,351; total, 4,033.

Attention may be called to the fact that in 1929 the former Division of Venereal Diseases of the State Board of Health was abolished and this work was placed under the Division of Preventable Diseases.

OF GENERAL INTEREST

Dr. N. Logan Leven has announced the opening of an office at 927 Lowry Medical Arts Building, Saint Paul, for the practice of surgery.

Dr. James J. Swendson of Saint Paul was elected a Fellow of the American College of Surgeons at the recent meeting of that organization in Chicago.

Dr. C. W. del Plaine, after serving as resident surgeon at the Miller Hospital, Saint Paul, has opened an office at 1942 Henepin Avenue, Minneapolis.

Dr. Francis W. Lynch has opened an office at 317 Lowry Medical Arts Building, Saint Paul, for the practice of medicine in caring for diseases of the skin and allied conditions.

Dr. Charles N. Spratt attended a meeting of the Pennsylvania State Medical Society in October, where he showed moving pictures of his methods of operating on glaucoma and cataract.

Dr. L. M. McQuire, heart specialist at the United States Veterans Hospital, Fort Snelling, has been transferred to Denver, where he will review the government pension cases for the balance of the year.

Dedication of the new nurses hall at the University of Minnesota was a feature of the annual homecoming program in October. The building was erected at a cost of $385,000 and has housing accommodations for 284 nurses.

Dr. E. S. Mariette of Glen Lake Sanatorium, Oak Terrace, Minnesota, presented a study on the student tuberculosis problem and a clinic on the use of x-ray in diagnosing tuberculosis at the recent meeting of the Mississippi Valley Conference on Tuberculosis held in Kansas City, Missouri.

Last month an oriental, D. Yomogita, claiming to have an M.D. and a Ph.D. degree, and stating that he was inspecting the mental hospitals of this country, left rather unexpectedly after having been taken to the state hospital at St. Peter. His claim to be conversant with several languages was not substantiated. His real purpose seemed difficult to construe.

The organization in Minneapolis of a naval reserve medical unit, to be known as United States Naval Hospital Unit No. 7, has been begun by Dr. C. E. Henry, who formed and commanded the Minneapolis unit in the World War. The new unit, which is to be formed for service only in an emergency—in the event of war—will be the first formed in the Northwest since the World War. Dr. Henry received authority from the headquarters of the ninth naval district at Great Lakes station to secure applications for the unit.

R. G. Leland, Chicago, director of the Bureau of Medical Economics of the American Medical Association, spent Monday, October 16, in the Twin Cities consulting with medical society officials.

He attended a noon luncheon conference with the executive committee of Hennepin County Medical Society and an afternoon conference in Saint Paul with officers of the Ramsey County Medical Society. He left for the West in the evening following a dinner in his honor at the Nicollet hotel in Minneapolis arranged by E. A. Meyerding, secretary of the State Association.

MINNESOTA STATE BOARD OF MEDICAL EXAMINERS

UNLICENSED PHYSICIAN PLEADS GUILTY TO PRACTICING MEDICINE

State of Minnesota *vs.* John G. Halland

On September 9, 1933, John G. Halland, thirty-nine years of age, entered a plea of guilty to practicing medicine without a license, before the Honorable Anton Thompson, Judge of the District Court, at Fergus Falls, Minnesota. Halland had been practicing medicine at Pelican Rapids, Minnesota, for two months without a license. The defendant formerly was licensed to practice medicine in the State of Minnesota, but his license was revoked in November, 1931, by the State Board of Medical Examiners, because of Halland's habitual indulgence in the use of narcotics.

Judge Thompson sentenced Halland to a six months term in the Otter Tail County jail. This sentence was suspended upon Halland's agreeing to return to his family home at Fargo, North Dakota, and upon his obeying the laws of the State of Minnesota, and also

A FORUM OF THE COMMITTEE ON PUBLIC HEALTH EDUCATION

Medical Care and Relief

FOR the first time on record a definite policy of paying from relief funds for medical service has been officially established. As a result, Federal Emergency Relief funds are now available for payment for medical care of the indigent in their homes and, in restricted instances, for care of ambulatory patients in the doctor's office.

This recognition of the legitimacy of the doctor's bill as compared with the bill of the grocer, the coal man, the landlord, is welcome and, in fact, overdue.

The detail involved in working out a satisfactory scheme for payment of medical service is another question and one which calls for the best thought of both physicians and relief agencies.

The question of what is a fair fee schedule for such work has been considered carefully and at length by representatives of the medical profession conferring with the state officials in charge of payment of funds. Their proposal is now ready for the consideration of physicians and it should be studied thoroughly.

It is doubtful if anyone will quarrel with the fees suggested for this service. In point of fact, many a physician has been performing the same services without any expectation of pay whatever, during the last two or three years. Often he has done it at considerable expense to himself.

Discussion of what constitutes a proper fee schedule will undoubtedly revolve instead about the propriety of sanctioning a set fee schedule at all.

Is the medical profession allowing itself to be definitely and officially committed to a schedule that can be enforced upon it at some future time when it is not a question of providing care for the needy but of providing care under some plan of state medicine for other groups of persons?

That question will be asked, and legitimately. At the same time the need for an established and understood basis for payment on the part of the relief agencies must not be forgotten; nor the needs of the unemployed for whom the funds were appropriated.

Nothing that the profession does for the sake of present policy and future contingencies must be allowed to stand in the way of the fullest possible utilization of these funds to care for the needy. The fact that there are people in remote counties who have been beyond the reach of medical service has been a matter of concern to the profession for some time. Physicians who might gladly have cared for these people without charge, had they been close by, have been unable to travel long distances at their own expense to aid them.

The new relief funds will allow mileage to the doctor as well as 50 per cent of a basic fee for home care of all such people.

The medical service thus financed is limited to home care and essential office care of ambulatory patients, though ambulatory patients will be directed when possible to whatever free clinics are available.

The policy to be followed in this matter by the government and government agencies as stated in the preamble to the rules and regulations will have the full approval and coöperation of the physicians. Note, for instance, the following paragraphs:

"It is hereby declared the policy of the Board of Control to recognize within the legal and economic limitations the traditional family and family-physician relationship in authorization of medical care for indigent persons in their homes and the traditional physician-nurse relationship in the authorization of bedside nursing care. The aim of these regulations shall be the provision of good medical service at a low cost—to the mutual benefit of the indigent patient, the physician, the nurse, the taxpayer. . . .

"In issuing these regulations, the Board of Control recognizes that no regulations can be all-inclusive and that many questions of interpretation will have to be referred to the Board for decision. In order to carry out this aim (above stated) the Board requests the full coöperation of the medical profession in observing the same high standard of professional ethics as is followed in their private practice."

the State of North Dakota. Judge Thompson made these conditions a part of the order suspending the sentence. A written report is to be submitted to the Court upon the first Monday in each month until November, 1934, showing the whereabouts and the occupation of the defendant.

The State Board of Medical Examiners acknowledges the splendid coöperation shown in this case by Mr. John L. Townley, Jr., County Attorney of Otter Tail County. The manner in which the case was disposed of by Judge Thompson indicates the fairness and frankness of the Court in this matter.

Petition Withdrawn to Operate Terpezone Institute

On September 18, 1933, the Saint Paul City Council held a public meeting to consider the rezoning of property at Hamline and Capitol Avenues in the City of Saint Paul. The purpose of the petition for rezoning the property was to enable certain people to operate what would have been known as the Hamline Clinic and Hospital. The petitioners were represented by Senator George L. Siegel, who stated that he was appearing for one Mr. J. J. Hicks, who is interested in the sale of Terpezone machines. These machines are purportedly for the treatment of tuberculosis and other respiratory ailments. The rezoning was opposed by Mr. Brist on behalf of the State Board of Medical Examiners and Ramsey County Medical Society. Mr. Edward A. Knapp also appeared in opposition on behalf of the Ramsey County Public Health Association.

Terpezone had previously been submitted to the Council on Pharmacy and Chemistry of the American Medical Association and was found "unacceptable for New and Non-official Remedies because no satisfactory evidence is presented to show that Terpezone is pinene ozonide or that in the manufacture of the product the formation of injurious by-products is controlled or prevented; because the claimed harmlessness of the product is not established, and because it is marketed with unwarranted and exaggerated claims of therapeutic value."

After hearing both sides and noting that the sentiment of the Council was not in favor of such a plan, Mr. Hicks personally withdrew his petition. The Minnesota State Board of Medical Examiners has taken the stand that the use of Terpezone to treat tuberculosis or any other ailment, constitutes the practice of healing and as such, if used at all, can only be used by one licensed to practice medicine and healing in the State of Minnesota.

TO ALL MEMBERS OF THE MEDICAL PROFESSION

The Minnesota State Board of Medical Examiners has received several complaints concerning itinerant quacks and unlicensed practitioners of healing that are very difficult to handle due to the fact that these individuals remain in a locality only for a day or two. This is particularly true of eye swindlers, so-called Indian doctors and other fly by night quacks.

The Board is very anxious to assist the local authorities in the apprehension of these people. Within the last month the conviction of one of these individuals was secured through the prompt coöperation of a physician who notified the Board by long distance telephone, and it was possible to apprehend the defendant within twenty-four hours. Consequently, the Board would very much appreciate being promptly notified by telephone or telegraph of the presence of any such individuals in any community in this state.

Please call or wire the Minnesota State Board of Medical Examiners, 524 Lowry Medical Arts Building, St. Paul, Minnesota; telephone Cedar 0347.

OBITUARY

Dr. A. E. Voges
1879-1933

Dr. A. E. Voges died at his home at White Bear Lake, Minnesota, on October 21, 1933, at the age of fifty-four.

Dr. Voges was born in Saint Paul and received his medical degree from the University of Minnesota in 1904. He moved to White Bear in 1911, where he had since practiced. At one time he was health officer of White Bear, and for the past fourteen years had been a deputy coroner of Ramsey County. He was a member of the Elks Lodge of Stillwater and was also a Master Mason.

Dr. Voges is survived by his widow, a son, Richard, and a daughter, Dorothy.

Dr. Harold Lauritz Stolpestad
1879-1933

Dr. Harold L. Stolpestad, for many years a practicing physician in the Dayton's Bluff district of Saint Paul, died in his office on East Seventh Street, on October 18, 1933, at the age of fifty-six.

Born in Norway, Dr. Stolpestad came to Saint Paul as an infant and was educated in the public schools of Saint Paul. He received his M.D. degree at the University of Minnesota in 1902 and practiced for several years, following graduation, in Saint Paul before moving to Lafayette, Minnesota. He later returned to Saint Paul where he joined the Ramsey County Medical Society in 1911.

Dr. Stolpestad is survived by his widow and two sons, Dr. Herbert L. Stolpestad and Dr. Armer H. Stolpestad, both of whom graduated from the medical school of the University of Minnesota in June, 1933.

Dr. Frank E. Balcome
1872-1933

Dr. Frank E. Balcome, a practicing physician in Saint Paul for thirty-five years, died at the Midway Hospital on October 21, 1933, following an illness of two weeks.

Born at Delano, Minnesota, in 1872, the son of Dr. Edwin Balcome, he moved to Howard Lake as a boy in 1876. After graduating from Macalester College in 1895 he began the study of medicine at the University of Minnesota and completed the course at the Eclectic Medical Institute of Cincinnati, Ohio, in 1899.

Upon beginning practice in Saint Paul Dr. Balcome soon became associated with Dr. C. M. Cannon at St. Anthony Park, Saint Paul, and continued to practice in Saint Paul until his death, his office in recent years being at University and Snelling Avenues.

Dr. Balcome joined the Ramsey County Medical Society, September 25, 1905, and was thus a member of the Minnesota State Medical Association and the American Medical Association. He was also a Mason and Odd Fellow.

In 1900 Dr. Balcome married Miss Anna M. Lutz of San Francisco. He is survived by his widow, three daughters, Ruth M., Jean W. and Marion Elizabeth, and a son, Milton M. Balcome.

FORTIFICATION OF FOODS OTHER THAN TABLE SALT WITH IODINE OR IODINE COMPOUNDS

The Committee on Foods reports that the fortification of foods other than table salt with iodine or iodine compounds may lead to excessive iodine intake and endanger public health. Foods so fortified, other than table salt, will not be eligible for acceptance. (Jour. A. M. A., August 5, 1933, p. 448.)

REPORTS AND ANNOUNCEMENTS OF SOCIETIES

MEDICAL BROADCAST FOR THE MONTH

The Minnesota State Medical Association Morning Health Service

The Minnesota State Medical Association broadcasts weekly at 11:15 o'clock every Wednesday morning over Station WCCO, Minneapolis and Saint Paul (810 kilocycles or 370.2 meters).

Speaker: William A. O'Brien, M.D., Associate Professor of Pathology and Preventive Medicine, Medical School, University of Minnesota.

The program for the month of November will be as follows:

November 1—Hardening of the Arteries.
November 8—Do Germs Cause Disease?
November 15—Sugar Hunger.
November 22—Problems of the Premature Infant.
November 29—History of Cancer.

SOUTHERN MINNESOTA MEDICAL ASSOCIATION

The forty-first annual meeting of the Southern Minnesota Medical Association was held at New Ulm, September 25, 1933. Turner Hall proved well adapted to the needs of the meeting with its small rooms for demonstrations, lounging room for commercial exhibit, auditorium and basement beer garden.

There were some 179 registrations out of a membership of 400. Professor C. O. Rosendahl and R. V. Ellis of the University, who had received the medal for their scientific exhibit at the State Association meeting, were presented at the luncheon meeting, as was also Dr. Lloyd Whitesell, the recipient of the hundred dollar award to the senior student at the University. The applications of twenty-one new members were accepted.

The officers elected for the coming year were: Dr. M. C. Piper, Rochester, president; Dr. S. A. Slater, Worthington, first vice president; Dr. W. G. Workman, Tracy, second vice president; Dr. H. C. Habein, Rochester, secretary-treasurer.

The next annual meeting will probably be held at Mankato.

STATE MEETING—1934

Preparations are already under way for the 81st Annual Meeting of the Minnesota State Medical Association following the first meeting of the 1933-34 Committee on Scientific Assembly held at the Lowry Hotel in Saint Paul, September 30. The State Meeting is scheduled for July 16, 17 and 18, 1934, in Duluth.

A call for papers on new developments of any sort in medicine has been issued by the committee. Any new moving pictures, demonstrations and exhibits prepared by the members will also be welcomed by the committee in making up the 1934 scientific program.

The general plan for the meeting calls for two mornings of clinical and table demonstrations, Monday and Tuesday, with the afternoons of the same days devoted to papers. Wednesday, according to the present tentative plan, is to be given over to special society programs. The House of Delegates and Council meetings will probably precede the scientific program on Sunday.

The usual Monday night medical economics program will give place to a scientific program, possibly a cancer symposium, if present plans materialize. There will be a banquet Tuesday evening. All sessions of the meeting will be held at the Duluth Hotel and limitations of space will dictate to some extent the character of the program.

The demonstrations which have proved so popular at the last two state meetings will be emphasized again. Prominent among them in 1934 is to be a heart demonstration. Among other subjects under consideration for demonstrations or papers are neurogenic tumors; treatment of cyanide poisoning; agranulocytosis from barbiturates; newer concepts of lead poisoning and toxicology in general; pernicious anemia and treatment of all the anemias that do not respond to liver therapy; malnutrition among children; diabetes; cancer; adrenal surgery; varicose veins; hemorrhoids; fractures; minor surgery; and skin diseases.

Several distinguished out-of-state speakers will be invited to present papers or clinical and table demonstrations.

The 1934 committee is composed of: Section on Medicine: E. T. Herrmann, Saint Paul, chairman; R. E. Nutting, Duluth, secretary; Section on Surgery: W. D. White, Minneapolis, chairman; J. de J. Pemberton, Rochester, secretary; Clinical Demonstrations, W. A. O'Brien, Minneapolis.

The committee will meet again Saturday, November 4, at the Lowry Hotel, the Medical and Surgical Sections meeting at 5 P. M., to be joined by the others for dinner at 6:30.

BOOK REVIEWS

Books listed here become the property of the Ramsey and Hennepin County Medical libraries when reviewed. Members, however, are urged to write reviews of any or every recent book which may be of interest to physicians.

MINOR MALADIES AND THEIR TREATMENT. Leonard Williams, M.D. Sixth Edition. 420 pages. Price, cloth, $3.75. Baltimore: William Wood & Co., 1933.

FOOD, NUTRITION AND HEALTH. E. V. McCollum, Ph.D., Sc.D., and J. Ernestine Becker, M.A. Third Edition rewritten. 146 pages. Price $1.50, cloth. Baltimore, Md.: E. V. McCollum and J. Ernestine Becker, 1933.

INFECTION OF THE HAND. Allen B. Kanavel, M.D., Sc.D. Professor of Surgery, Northwestern University Medical School, etc. 552 pages. Illus. Price, $6.00, cloth. Philadelphia: Lea & Febiger, 1933.

THE TECHNIC OF LOCAL ANESTHESIA. Arthur E. Hertzler, M.D., Professor of Surgery, University of Kansas. Fifth Edition. 292 pages. Illus. Price, $5.00, cloth. St. Louis: C. V. Mosby Company, 1933.

WHEAT, EGG OR MILK FREE DIETS WITH RECIPES AND FOOD LISTS. Ray M. Balyeat, assisted by Elmer M. Rusten and Ralph Nowen. Philadelphia: J. B. Lippincott Co., 1933.

Eggs, wheat and milk have become notorious as causes of allergic reactions. However, being the basis of the ordinary North American diet, they are particularly difficult to avoid. Balyeat has, therefore, prepared this small book consisting mostly of recipes. The recipes apparently are well chosen and successful; in fact the reviewer's cook tried some of them successfully. There is also a short discussion of allergy in general and some of the allergic diseases in particular which seems a little heavy for the ordinary lay reader, and a little light for most doctors. There are tables of weights and blank sheets for diet diaries with reminders of unthought-of occurrences of milk, wheat and eggs. The book seems most useful for dietitians and particularly intelligent patients.

H. B. SWEETSER, JR., M.D.